

Table S1. SLiMs detected by the ELM resource within RHES regions: (A) N-terminal sequence, (B) Ras domain and (C) C-terminal tail.

A, N-terminal sequence						
Elm motif name	Instances (Matched Sequence)	Positions	Elm description	Cell compartment	Pattern	E-value
MOD_NEK2_1	MMKTLS	1-6	NEK2 phosphorylation motif with preferred Phe, Leu or Met in the -3 position to compensate for less favourable residues in the +1 and +2 position.	Nucleus, Cytosol, Centrosome, Ndc80 complex, Condensed nuclear chromosome outer kinetochore	[FLM][^P][^P]((ST))[^DEP][^DE]	9.798x10 <sup>-03</sup>
MOD_GSK3_1	TLSSGNCT	4-11	GSK3 phosphorylation recognition site	Cytosol, nucleus	...(ST)...[ST]	2.679x10 <sup>-02</sup>
MOD_Plk_1	GNCTLSV	8-14	Ser/Thr residue phosphorylated by the Plk1 kinase	Centralspindlin complex, Nucleus, Spindle, Gamma-tubulin complex, Midbody, Cytosol, Kinetochore, Spindle midzone, Nuclear condensin complex, Cleavage furrow, Nucleoplasm, Microtubule organizing center	[DNE][^PG][ST]((FYILMVV[.]) (^PEDGKN) FWYLIVM))	7.674x10 <sup>-03</sup>
LIG_FHA_1	NCTLSVP	9-15	Phosphothreonine motif binding a subset of FHA domains that show a preference for a large aliphatic amino acid at the pT+3 position.	Nucleus	..(T).[ILV].	8.662x10 <sup>-03</sup>
DOC_PP2B_LxvP_1	LSVP	12-15	Docking motif in calcineurin substrates that binds at the interface of the catalytic CNA and regulatory CNB subunits.	Cytosol, Calcineurin complex, Nucleus	L.[LLIVAPM]P	2.296x10 <sup>-03</sup>

Table SI. Continued.

Elm name	Positions	Elm description	Cell compartment	Pattern
DOC_USP7_MATH_1	16-20	The USP7 MATH domain binding motif variant based on the MDM2 and p53 interactions.	Nucleus	[PA][^P][^FYWIL]S[^P]
LIG_LIR_Gen_1	19-23 92-97 104-109 105-109 180-186 181-186	Canonical LIR motif that binds to Atg8 protein family members to mediate processes involved in autophagy.	Cytosol, Cytoplasmic side of late Endosome membrane	[EDST].{0,2}[WFY]. [ILV]
TRG_ENDOCYTIC_2	20-23 168-171 184-187	Tyrosine-based sorting signal responsible for the interaction with mu subunit of AP (Adaptor Protein) complex	Plasma membrane, Clathrin-coated endocytic vesicle, cytosol	Y.[LMVIF]
MOD_NEK2_1	25-30 72-77 169-174	NEK2 phosphorylation motif with preferred Phe, Leu or Met in the -3 position to compensate for less favourable residues in the +1 and +2 position.	Nucleus, Cytosol, Centrosome, Ndc80 complex, Condensed nuclear chromosome outer Kinetochores	[FLM][^P][^P](ST) [^DEP][^DE]
LIG_14-3-3_CanoR_1	29-39	Canonical Arg-containing phospho-motif mediating a strong interaction with 14-3-3 proteins.	Nucleus, Internal side of plasma membrane, Cytosol	R[^DE]{0,2}[^DEPG] (ST)([FWYLMV]). ([^PRIKGN]P) ([^PRIKGN]{2,4} [VILMFWY]) ..(ST)...[ST]
MOD_GSK3_1	30-37	GSK3 phosphorylation recognition site	Cytosol, Nucleus	.[^IRFW](ST) [ILMVFWY] [ILMVFWY].
MOD_Plk_4	31-37 84-90	Ser/Thr residue phosphorylated by Plk4	Cytosol, SCF ubiquitin ligase complex, Cleavage furrow, Centriole, Gamma-tubulin ring complex, centriolar Satellite, Pericentriolar material	
MOD_CK1_1	34-40 87-93	CK1 phosphorylation site	Cytosol, Nucleus	S..(ST)...

Table S1. Continued.

EIm name	Positions	EIm description	Cell compartment	Pattern
LIG_PTB_Apo_2	38-45	These phosphorylation-independent motifs bind to Dab-like PTB domains. Binding is not driven by contacts at the O or FY position, but instead is dependent upon the large number of hydrophobic and hydrogen bond contacts between motif and domain.	Integrin, Internal side of plasma membrane, Cytosol, Receptor complex, Cytoplasmic membrane-bounded vesicle	([ <sup>^</sup> P].NP.[FY].)  {.}[ILV]MFY N..[FY].)
DOC_WW_Pin1_4	46-51	The Class IV WW domain interaction motif is recognised primarily by the Pin1 phosphorylation-dependent prolyl isomerase.	Nucleus,	...([ST])P.
MOD_ProDKin_1	46-52	Proline-Directed Kinase (e.g. MAPK) phosphorylation site in higher eukaryotes.	Cytosol, Nucleus	...([ST])P..
DOC_CKSI_1	47-52	Phospho-dependent motif that mediates docking of CDK substrates and regulators to cyclin-CDK-bound Cks1.	Cytosol, Nucleus	[MPVLIFWYQ].(T)P..
LIG_FHA_1	47-53	Phosphothreonine motif binding a subset of FHA domains that show a preference for a large aliphatic amino acid at the pT+3 position.	Nucleus	..(T)..[ILV].
LIG_SH2_STAT5	48-51 168-171 184-187	STAT5 Src Homology 2 domain binding motif.	Cytosol	(Y)[VLTFC]..
LIG_FHA_2	49-55 152-158 175-181	Phosphothreonine motif binding a subset of FHA domains that prefer an acidic amino acid at the pT+3 position.	Nucleus, Replication fork	..(T)..[DE].
LIG_WD40_WDR5_VDV_1	65-71	This WDR5-binding motif binds to a cleft between blades 5 and 6 of the WD40 repeat domain of WDR5, opposite of the Win motif-binding site, to mediate assembly of histone modification complexes.	Nucleus, Histone methyltransferase complex	[ED].{0,3}[VIL]D[VI]
TRG_ER_diArg_1	83-85 84-86	The di-Arg ER retention motif is defined by two consecutive arginine residues or with a single residue insertion. The motif is completed by an adjacent hydrophobic/arginine residue which may be on either side of the Arg pair.	Endoplasmic reticulum membrane, Integral protein, ER-Golgi transport vesicle membrane, Endoplasmic reticulum membrane, Golgi-ER transport vesicle membrane, Rough endoplasmic reticulum, Endoplasmic reticulum cisterna, cytosol	([LIV]MFYWPR] R[ <sup>^</sup> YFWDE] {0,1}R)(R[ <sup>^</sup> YFWDE] {0,1}R [LIV]MFYWPR])
MOD_PK_1	84-90	Phosphorylase kinase phosphorylation site	Cytosol	[RK]..(S)[VI]..
MOD_PKA_2	84-90 102-108	Secondary preference for PKA-type AGC kinase phosphorylation.	Cytosol, Nucleus, cAMP-dependent protein kinase complex	..R..([ST])[ <sup>^</sup> P]..
MOD_PKA_1	84-90 174-180	Main preference for PKA-type AGC kinase phosphorylation.	cAMP-dependent protein kinase complex, Cytosol, Nucleus	[RK] RK .([ST])[ <sup>^</sup> P]..

Table SI. Continued.

Elm name	Positions	Elm description	Cell compartment	Pattern
TRG_LysEnd_APsAcLL_1	92-97 155-160	Sorting and internalisation signal found in the cytoplasmic juxta-membrane region of type I transmembrane proteins. Targets them from the Trans Golgi Network to the lysosomal-endosomal-melanosomal compartments. Interacts with adaptor protein complexes	Cytosol, Endocytic vesicle	[DERQ]...L[LV]
LIG_Pex14_2	94-98 183-187	Fxxx[WF] motifs are present in Pex19 and <i>S. cerevisiae</i> Pex5 cytosolic receptors that bind to peroxisomal membrane docking member, Pex14	Cytosol, Peroxisome, Glycosome	F...[WF]
MOD_CK2_1	102-108 151-157 158-164	CK2 phosphorylation site	Nucleus, Cytosol, Protein kinase CK2 complex	...(ST)..E
MOD_SUMO_rev_2	104-112 105-112 107-112	Inverted version of SUMOylation motif recognized for modification by SUMO-1	PML body, Nucleus	[SDE]{0,5}[DE].(K). {0,1}[AIFLMPSTV]
DOC_MAPK_gen_1	110-119 111-119	MAPK interacting molecules (e.g. MAPKKs, substrates, phosphatases) carry docking motif that help to regulate specific interaction in the MAPK cascade. The classic motif approximates (R/K)xxxx#x# where # is a hydrophobic residue.	Nucleus, Cytosol	[KR]{0,2}[KR].{0,2} [KR].{2,4}[ILVM]. [ILVF]
DOC_USP7_UBL2_3	110-114 120-124 124-128	The USP7 CTD domain binding motif variant based on the ICP0 and DNMT1 interactions	Nucleus	K...K
LIG_SUMO_SIM_par_1	115-121	Motif for the parallel beta augmentation mode of non-covalent binding to SUMO protein.	PML body, Nucleus, Nuclear body	[DEST]{0,5}. [VILPTM][VIL] [DESTVILMA][VIL]. {0,1}[DEST]{1,10} [ILM][ILMF].{1,2} [ILM].{0,4}K
LIG_UBA3_1	182-191 186-191	UBA3 adenylation domain binding motif variant based on the UBE2M and UBE2F interactions.	Nucleus	

Table SI. Continued.

Elm motif name	Instances (Matched Sequence)	Positions	Elm description	Cell compartment	Pattern	E-value
DOC_WW_Pin1_4	HEMSPA GMVSPF	194-199 229-234	The Class IV WW domain interaction motif is recognised primarily by the Pin1 phosphorylation-dependent prolyl isomerase.	Nucleus, Cytosol	...(ST)P.	1.543x10 <sup>-02</sup>
MOD_ProDKin_1	HEMSPAL GMVSPFA	194-200 229-235	Proline-Directed Kinase (e.g. MAPK) phosphorylation site in higher eukaryotes.	Cytosol, Nucleus	...	1.543x10 <sup>-02</sup>
LIG_14-3-3_CanoR_1	RKISVQ	202-207	Canonical Arg-containing phospho-motif mediating a strong interaction with 14-3-3 proteins.	Nucleus, Internal side of plasma membrane, Cytosol	R[^A]DE[0,2][^A]DEPG[0,1]([FWYLMV])([^A]PRIKGN[IP])([^A]PRIKGN){2,4}[VILMFWYPI]) [RK].(S)[VI]..	4.477x10 <sup>-03</sup>
MOD_PK_1	RKISVQY RRPSVNS	202-208 236-242	Phosphorylase kinase phosphorylation site	Cytosol	...	9.418x10 <sup>-04</sup>
MOD_PKA_1	RKISVQY RRPSVNS	202-208 236-242	Main preference for PKA-type AGC kinase phosphorylation.	cAMP-dependent protein kinase Complex, Cytosol, nucleus	[RK][RK].(ST)[^A]P]..	2.315x10 <sup>-03</sup>
TRG_ER_diArg_1	MRR RRV RRP	219-221 220-222 236-238	The di-Arg ER retention motif is defined by two consecutive arginine residues or with a single residue insertion. The motif is completed by an adjacent hydrophobic/arginine residue which may be on either side of the Arg pair.	Endoplasmic reticulum membrane, Integral protein, ER-Golgi transport vesicle membrane, Endoplasmic reticulum membrane, Golgi-ER transport vesicle membrane, Rough endoplasmic reticulum, Endoplasmic reticulum cisterna, cytosol	(LIVMFYWPR] R[^A]YFWDE[0,1}R) R[^A]YFWDE[0,1} R[LIVMFYWPR]	5.369x10 <sup>-03</sup>
LIG_LIR_Gen_1	DAYGMV	226-231	Canonical LIR motif that binds to Atg8 protein family members to mediate processes involved in autophagy.	Cytosol, Cytoplasmic side of late endosome Membrane	[EDST]{0,2}[WFY].-[ILV]	5.200x10 <sup>-03</sup>
TRG_ENDOCYTIC_2	YGMV	228-231	Tyrosine-based sorting signal responsible for the interaction with mu subunit of Adaptor Protein complex	Plasma membrane, Clathrin-coated endocytic vesicle, Cytosol	Y.[LMVIF]	2.587x10 <sup>-03</sup>
MOD_CDK_SPxxK_3	GMVSPFAR	229-236	Longer version of the CDK phosphorylation site which shows specificity towards a lysine/arginine residue at position +4 after the phospho-Ser/Thr	Cycloplasmic cyclin-dependent protein Kinase holoenzyme complex, Origin recognition complex, Spindle, Microtubule, Cytosol, Nucleus	...(ST)P.[RK]	1.929x10 <sup>-03</sup>

Table SI. Continued.

Elm motif name	Instances (Matched Sequence)	Positions	Elm description	Cell compartment	Pattern	E-value
MOD_PKA_2	RRPSVNS	236-242	Secondary preference for PKA-type AGC kinase phosphorylation.	Cytosol, Nucleus, cAMP-dependent protein kinase Complex	.R.(^ST) ^P ..	9.458x10 <sup>-03</sup>
MOD_CK1_1	SVNSDLK	239-245	CK1 phosphorylation site	Cytosol, Nucleus	S.(^ST)...	1.704x10 <sup>-02</sup>
MOD_SUMO_rev_2	SVNSDLKYI	239-247	Inverted version of SUMOylation motif	PML body, Nucleus	[SDE]{0,5}[DE](K){0,1}	1.280x10 <sup>-02</sup>
LIG_Actin_WH2_2	SDLKYI	242-247	recognized for modification by SUMO-1	Nucleus	[AIFLMPSTV]	6.603x10 <sup>-04</sup>
	VNSDLKYIK AKVLREG	240-255	The WH2 motif is of variable length (16-19 amino acids) binding to the hydrophobic cleft formed by actin's subdomains 1 and 3. At the N-terminus it forms an $\alpha$ -helix followed by a flexible loop stabilised upon actin binding.	Cytosol	[^R].(^[ILMVV]) ([ILMVV]) [^P] ^P ([LVM]){4,7}L([IKR])  (NK) VATIGS]	
LIG_SH2_STAT5	YIKA	246-249	STAT5 Src Homology 2 domain binding motif.	Cytosol	(Y) VLTFC ..	3.296x10 <sup>-03</sup>
MOD_CAAAXbox	CTIQ	263-266	Generic CAAAX box phosphorylation motif	Cytosol	(C) ^DENQ LIVMF .\$	2.446x10 <sup>-06</sup>