

## **Tools & Databases of Short Linear Motifs**

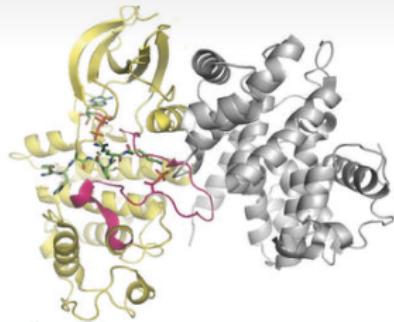
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Holger Dinkel

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EMBO Practical Course Computational analysis of protein-protein interactions: From sequences to networks

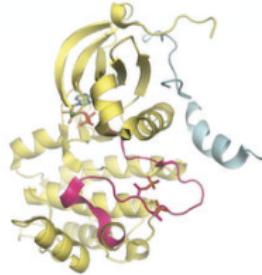
## PROTEIN PHOSPHORYLATION SITES



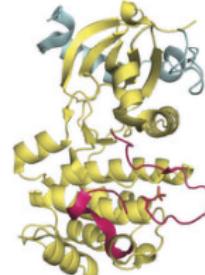
Cdk1/cyclin B



Plk1



Aurora A/TPX2



Aurora B/INCENP

*"Spatial exclusivity combined with positive and negative selection of phosphorylation motifs is the basis for context-dependent mitotic signaling"; ALEXANDER ET AL.; (SCI. SIG 2011)*

Tools & Databases of Short Linear Motifs

## PROTEIN PHOSPHORYLATION SITES

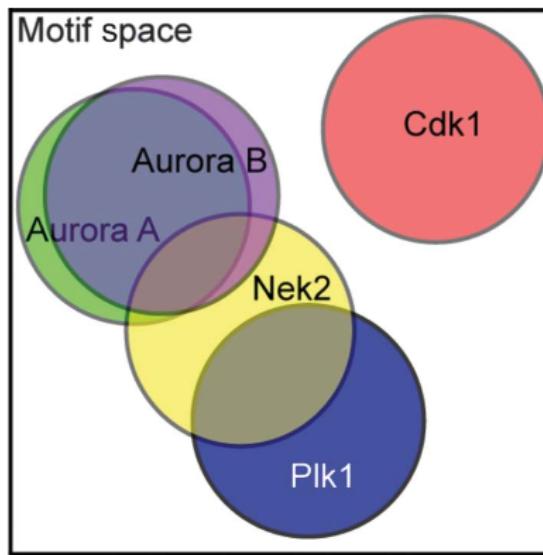
Kinase	-3	-2	-1	0	1	2	3
Cdk1	.	.	.	p[ST]	P	.	[KR]
Plk1	.	[DEN]	.	p[ST]	[ILMVFWY]	.	.
Nek2	[FML]	[!P]	[!P]	p[ST]	[ILMV]	.	.
AuroraA	R	[KR]	.	p[ST]	[!P]	.	.
AuroraB	.	R	[KR]	p[ST]	[!P]	.	.

"Spatial exclusivity combined with positive and negative selection of phosphorylation motifs is the basis for context-dependent mitotic signaling"; ALEXANDER ET AL.; (SCI. SIG 2011)

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## PROTEIN PHOSPHORYLATION SITES

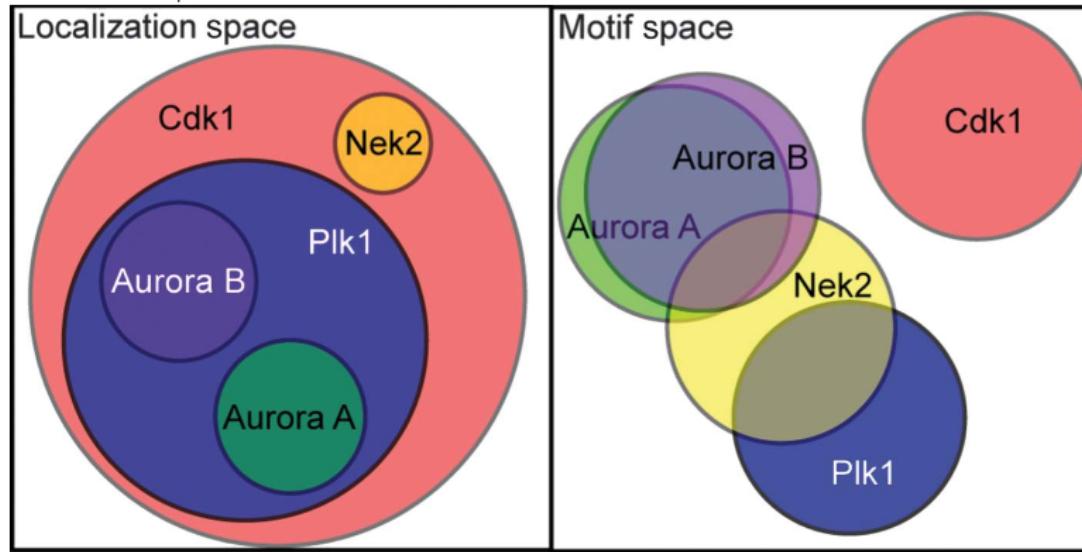
Kinase	-3	-2	-1	0	1	2	3
Cdk1	.	.	.	p[ST]	P	.	[KR]
Plk1	.	[DEN]	.	p[ST]	[ILMVFWY]	.	.
Nek2	[FML]	[!P]	[!P]	p[ST]	[ILMV]	.	.
AuroraA	R	[KR]	.	p[ST]	[!P]	.	.
AuroraB	.	R	[KR]	p[ST]	[!P]	.	.



"Spatial exclusivity combined with positive and negative selection of phosphorylation motifs is the basis for context-dependent mitotic signaling"; ALEXANDER ET AL.; (SCI. SIG 2011)

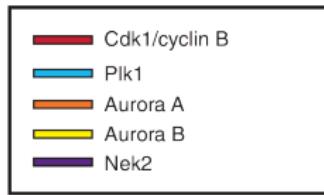
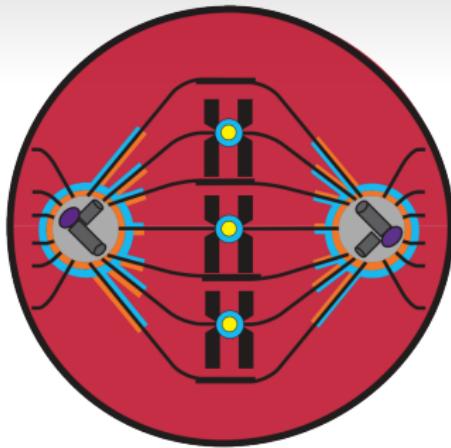
## PROTEIN PHOSPHORYLATION SITES

Kinase	-3	-2	-1	0	1	2	3
Cdk1	.	.	.	p[ST]	P	.	[KR]
Plk1	.	[DEN]	.	p[ST]	[ILMVFWY]	.	.
Nek2	[FML]	[!P]	[!P]	p[ST]	[ILMV]	.	.
AuroraA	R	[KR]	.	p[ST]	[!P]	.	.
AuroraB	.	R	[KR]	p[ST]	[!P]	.	.



"Spatial exclusivity combined with positive and negative selection of phosphorylation motifs is the basis for context-dependent mitotic signaling"; ALEXANDER ET AL.; (SCI. SIG 2011)

# PROTEIN PHOSPHORYLATION SITES



Kinase localization in Metaphase:

**Cdk1** whole cell

**Plk1** kinetochores

**Aurora A** centrosomes & microtubules

**Aurora B** centromeres & spindle

**Nek2** centrosomes

## Phospho.ELM

Database of experimentally verified phosphorylation sites in eukaryotic proteins.

Current release contains 8,718 protein entries covering more than 42,500 instances. (Instances are fully linked to literature references.)

# Phospho.ELM

a database of S/T/Y phosphorylation sites

Statistics:

Instances	42,575
Kinases	310
Reference	3,672
Sequences	11,223
Substrates	8,718

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## SEARCH

- for phosphorylation sites in proteins using protein name or gene name  
(eg. Paxillin, Shc, MAPK)

- by UniPROT accession or Ensembl identifier:  
(eg. P12931 or P55211)

- by selected kinase (List):

 +

- by selected phospho-peptide binding domain (List):

 +

- Choose which organisms to include

All
Caenorhabditis
Drosophila
Vertebrates

- Do not show high throughput data

- Output as Comma-Separated-Values (.csv)

# Phospho.ELM

a database of S/T/Y phosphorylation sites

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Substrate: p53 (Cellular tumor antigen p53)

Seq-ID: P04637 [*Homo sapiens*]

Interaction Network(s): STRING NetworkKin

External Source(s): PHOSIDA

MINT Interaction(s): [\[show\]](#)GO-Terms: [\[show\]](#)

Conservation:

● Click on table headers for sorting

Res.	Pos.	Sequence	Kinase	PMID	Src	Cons.	ELM	Binding Domain	SMART/Pfam	IUPRED score	PDB	P3D Acc.
S	9	MEEPQSDP <b>S</b> VEPPLSQETF	-	11875057	LTP	0.75		-	P53_TAD	0.94	-	-
S	15	QSDPSVEPPL <b>S</b> QETFSDLWKL	DNA-PK	10446957	LTP	1.00	MOD_PIKK_1	-	P53_TAD	0.66	-	-
S	15	QSDPSVEPPL <b>S</b> QETFSDLWKL	ATM	11875057	LTP	1.00	MOD_PIKK_1	-	P53_TAD	0.66	-	-
T	18	PSVEPPLSQ <b>T</b> FSDLWKLPE	CK1_group	10606744	LTP	1.00	MOD_CK1_1	-	P53_TAD	0.66	-	-
T	18	PSVEPPLSQ <b>T</b> FSDLWKLPE	TTK	19332559	LTP	1.00	MOD_CK1_1	-	P53_TAD	0.66	-	-
T	18	PSVEPPLSQ <b>T</b> FSDLWKLPE	VRK1	10951572	LTP	1.00	MOD_CK1_1	-	P53_TAD	0.66	-	-
T	18	PSVEPPLSQ <b>T</b> FSDLWKLPE	VRK1	15542844	LTP	1.00	MOD_CK1_1	-	P53_TAD	0.66	-	-
S	20	VEPPLSQ <b>T</b> TFSDLWKLPENN	-	15254178	LTP	0.95		-	P53_TAD	0.58	-	-
S	20	VEPPLSQ <b>T</b> TFSDLWKLPENN	-	15489221	LTP	0.95		-	P53_TAD	0.58	-	-
S	20	VEPPLSQ <b>T</b> TFSDLWKLPENN	-	10801407	LTP	0.95	-	P53_TAD	0.58	-	-	
S	20	VEPPLSQ <b>T</b> TFSDLWKLPENN	-	12111733	LTP	0.95	-	P53_TAD	0.58	-	-	

# Phospho.ELM

a database of S/T/Y phosphorylation sites

Substrate: Cyclin dependent kinase inhibitor 1B (Cyclin-dependent kinase inhibitor 1B (Cyclin-dependent kinase p46527 [Homo sapiens])  
 Seq-ID: 54994299  
 Interaction Network(s): BioGRID, NetworkKit  
 External Sources: MINT Interactions: [show]  
[View Conservation](#)

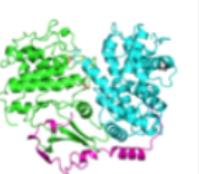
Res. #	Pos. #	Sequence	Kinase	PMID #	Src	Cons. #	ELM	Binding Domains	SMART/Plnts	IPRED score	PDB	PID Acc.
S	10	R <b>E</b> S <b>D</b> T <b>I</b> G <b>L</b> <b>A</b> <b>R</b> <b>G</b> <b>A</b> <b>R</b> <b>G</b>	-	13440295	LTP	0.28	-	-	-	0.74	-	-
S	10	R <b>E</b> S <b>D</b> T <b>I</b> G <b>L</b> <b>A</b> <b>R</b> <b>G</b> <b>A</b> <b>R</b> <b>G</b>	-	14504289	LTP	0.28	-	-	-	0.74	-	-
S	10	R <b>E</b> S <b>D</b> T <b>I</b> G <b>L</b> <b>A</b> <b>R</b> <b>G</b> <b>A</b> <b>R</b> <b>G</b>	-	187305731	LTP	0.28	-	-	-	0.74	-	-
S	10	R <b>E</b> S <b>D</b> T <b>I</b> G <b>L</b> <b>A</b> <b>R</b> <b>G</b> <b>A</b> <b>R</b> <b>G</b>	-	12042014	LTP	0.28	-	-	-	0.74	-	-
S	10	R <b>E</b> S <b>D</b> T <b>I</b> G <b>L</b> <b>A</b> <b>R</b> <b>G</b> <b>A</b> <b>R</b> <b>G</b>	-	15302935	LTP	0.28	-	-	-	0.74	-	-
S	10	R <b>E</b> S <b>D</b> T <b>I</b> G <b>L</b> <b>A</b> <b>R</b> <b>G</b> <b>A</b> <b>R</b> <b>G</b>	PKB_group	16760593	LTP	0.28	-	-	-	0.74	-	-
S	10	R <b>E</b> S <b>D</b> T <b>I</b> G <b>L</b> <b>A</b> <b>R</b> <b>G</b> <b>A</b> <b>R</b> <b>G</b>	KIS	12003740	LTP	0.28	-	-	-	0.74	-	-
Y	74	F <b>R</b> E <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	-	18454177	LTP	1.00	-	-	-	0.64	-	-
Y	74	F <b>R</b> E <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	SRC	17254967	LTP	1.00	-	-	-	0.64	-	-
S	83	E <b>R</b> E <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	-	16634093	LTP	0.18	MOD_CK2_1	-	-	0.57	1JBU	85.37%
Y	88	E <b>R</b> E <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	-	17254966	LTP	1.00	-	-	-	0.65	1JBU	70.31%
Y	88	E <b>R</b> E <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	-	18195327	LTP	1.00	-	-	-	0.65	1JBU	70.31%
Y	88	E <b>R</b> E <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	SRC	17254967	LTP	1.00	-	-	-	0.65	1JBU	70.31%
Y	89	E <b>R</b> E <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	-	16195327	LTP	0.22	-	-	-	0.63	1JBU	36.88%
Y	89	E <b>R</b> E <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	SRC	17254967	LTP	0.22	-	-	-	0.63	1JBU	36.88%
S	140	L <b>E</b> S <b>D</b> <b>T</b> <b>I</b> <b>G</b> <b>L</b> <b>A</b> <b>R</b> <b>G</b> <b>A</b> <b>R</b> <b>G</b>	-	17525532	HTTP	0.85	-	-	-	0.77	-	-
T	157	Q <b>C</b> E <b>D</b> <b>T</b> <b>I</b> <b>G</b> <b>L</b> <b>A</b> <b>R</b> <b>G</b> <b>A</b> <b>R</b> <b>G</b>	PKB_group	12042003	LTP	0.94	MOD_PKB_1	-	-	0.84	-	-
T	157	Q <b>C</b> E <b>D</b> <b>T</b> <b>I</b> <b>G</b> <b>L</b> <b>A</b> <b>R</b> <b>G</b> <b>A</b> <b>R</b> <b>G</b>	PKB_group	12240302	LTP	0.94	MOD_PKB_1	-	-	0.84	-	-
T	157	Q <b>C</b> E <b>D</b> <b>T</b> <b>I</b> <b>G</b> <b>L</b> <b>A</b> <b>R</b> <b>G</b> <b>A</b> <b>R</b> <b>G</b>	PKB_group	12240301	LTP	0.94	MOD_PKB_1	-	-	0.84	-	-
S	178	A <b>R</b> E <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	MAPK1	10831586	LTP	0.10	MOD_ProCK1	-	-	0.94	-	-
T	187	G <b>E</b> A <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	-	187305731	LTP	1.00	MOD_CDK_1	-	-	0.95	-	-
T	187	G <b>E</b> A <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	-	12042014	LTP	1.00	MOD_CDK_1	-	-	0.95	-	-
T	187	G <b>E</b> A <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	-	10831586	LTP	1.00	MOD_CDK_1	-	-	0.95	-	-
T	187	G <b>E</b> A <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	CDK2	12700233	LTP	1.00	MOD_CDK_1	-	-	0.95	-	-
T	188	F <b>R</b> E <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	-	12042014	LTP	0.00	-	YMMHQ	14-3-3	-	0.94	-
T	188	F <b>R</b> E <b>D</b> <b>G</b> <b>V</b> <b>E</b> <b>N</b> <b>E</b> <b>T</b> <b>E</b> <b>R</b> <b>S</b>	RSK_group	14504289	LTP	0.00	-	YMMHQ	14-3-3	-	0.94	-

Order tendency query sequence: 

MOD\_CK2\_1  
 The ELM server:  ELM details  
 CK2 phosphorylation site:  
 Motif recognized by CK2 for Ser/Thr phosphorylation  
 MOD\_CK2\_1  
 The main determinant of CK2 phosphorylation specificity is a negative charge 3 positions after the modification residue  
 Pattern: -3T-  
 Verbosity: Extensive Zax maps Saccharomyces cerevisiae Drosophila melanogaster  
 Not represented in taxonomy:

Click on table headers for sorting

PDB entry: 1jbu   
 P2TKP1USC1M A/CDK2 COMPLEX  
 Visualisation  
 PDB Viewer: View the PDB entry using [Atom viewer](#).  
 Jmol: View the PDB entry using [Jmol](#).  
 Open Atom: View the PDB entry using [Open Atom viewer](#).



**phospho3D** 

Base 1/125411 Documentations 1 Models 1 Links 1 Labels

p2TKP1USC1M A/CDK2 complex						
PIR code	Keywords	Complexes	Protein	PhosphoELM	Epitope	Site
C	141	1.0	18622	Interdomain	CDK2	141-17-29
C	141	3.0	18622	Interdomain	CDK2	141-17-29

**Links to:**

- STRING
- NetworKin
- Phosida
- Phospho3D

**Display:**

- MINT interactions
- GO-Terms

**Substrate:****Caspase 9** (Cysteine protease)**Seq-ID:****P55211** [*Homo sapiens*]**Interaction Network(s):****External Source(s):****PHOSIDA**[\[hide\]](#)

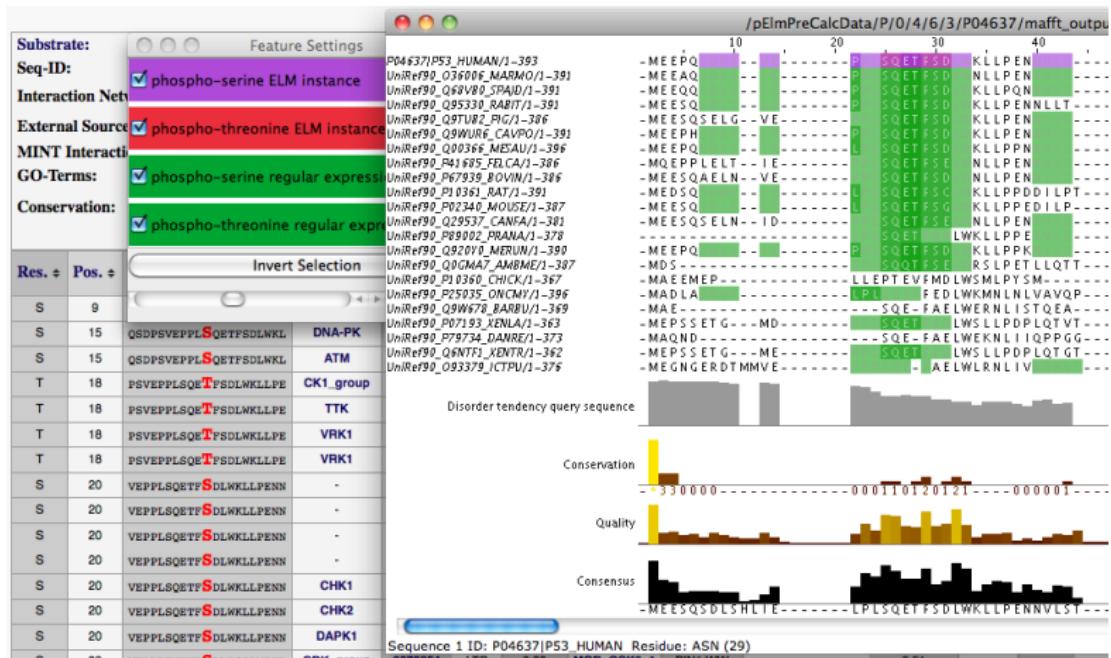
MINT-15372 APAF\_HUMAN

MINT-18815 CASP3\_HUMAN

MINT-25026 XIAP\_HUMAN

[\[hide\]](#)**MINT Interaction(s):****Molecular Function**cysteine-type endopeptidase activity,  
protein binding,  
enzyme activator activity**GO-Terms:**

Precalculated conservation scores for the phosphorylation sites are presented using **Jalview**





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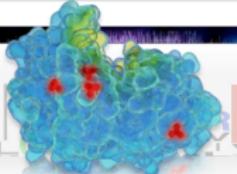
Cell Signaling  
TECHNOLOGY®

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Please cite the following reference for this resource: Hornbeck PV, et al. (2012) *Nucleic Acids Res.* 2012 40:D261-70. [reprint]

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Aug 2014 [Download PTM-VarMut dataset](#): Overlap of disease missense mutations & genetic variants, with their corresponding PTMs and flanking sequences.

Jul 2012 [Download Datasets of Regulatory or Disease-Associated Sites](#).

Dec 2011 [Download "PhosphoSitePlus: a comprehensive resource..."](#) in January 2012 issue of *Nucleic Acids Research*.

Jul 2011 [Multiple Sequence Alignment \(MSA\) added to the Protein Page](#).

Jul 2011 [Download PyMOL & Chimera Scripts](#) from the Structure Viewer window.

### Phosphorylation Site Statistics

Non-redundant sites:	239,738
Non-redundant proteins:	19,680
Sites curated from literature:	136,109
All sites using site-specific (SS) methods:	12,528
All sites using discovery-mode MS (MS) methods:	127,064
Sites using both SS and MS methods:	6,010
MS sites observed at CST:	151,472
Number of curated papers:	16,428

### Other Modification Site Statistics

Acetylation:	27,657	Caspase cleavage:	481
Di-methylation:	2,555	Methylation:	163
Mono-methylation:	4,992	O-GalNAc:	2,118
O-GlcNAc:	1,390	Succinylation:	4,657
Sumoylation:	816	Tri-methylation:	321
Ubiquitination:	51,255		



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Home		with grant support from NIAAA National Institute on Alcohol Abuse and Alcoholism									
		Cell Signaling TECHNOLOGY®									
Advanced Search / Browse Functions:											
Search Results for: p53											
Modification-specific Antibodies Available from Cell Signaling Technology® Protein-specific Antibodies or siRNA Available from Cell Signaling Technology®											
DISPLAYING 1-64 OF 64 RECORDS. << PREVIOUS   NEXT >>											
<b>Protein</b>	<b>GeneSymb</b>	<b>ACC#</b>	<b>Organism</b>	<b>MW (Da)</b>	<b>Modifications(show legend)</b>	<b>DOWNLOAD</b>					
p53		TP53	human	43,653							
		P04637	mouse	43,559							
		P04749	rat	43,451	H-m1, K-ac, K-m1, K-m2, K-sm, K-ub, R-m1, S-gl, S-p, T-p, Y-p						
		P10361	rabbit	43,451							
		Q93330	monkey	43,696							
		P13481									
S3BP1		TP53BP1	human	213,574	D-ca, K-ac, K-m1, K-ub, R-m1, S-p, T-p, Y-p						
tumor protein p53 binding protein 1		P70399	mouse	211,340							
		XP_215812	rat	212,859							
S3BP2		TP53BP2	human	125,616							
Apoptosis-stimulating of p53 protein 2		Q8CQ79	mouse	125,301							
		XP_215812	rat	125,301							
AIFM2		AIFM2	human	40,527	K-ac, K-ub, S-gl, S-p, T-p, Y-p						
		Q9BRQ8	mouse	40,635							
		Q8BU44	rat	90,267							
ANO9		ANO9	human	87,180	S-p, T-p, Y-p						
tumor protein p53 inducible protein 5		P86044	mouse	87,180							
		XP_574586	rat	98,746							
CDIP1		CDIP1	human	21,892							
		Q9H305	mouse	21,835	K-ub, T-p						
		Q9D875	rat	21,858							
CYFIP2		CYFIP2	human	148,398							
p53 inducible protein		Q5SCX6	mouse	145,659	K-ac, K-ub, S-p, T-p, Y-p						
		D3Z382	rat	68,079							
EFEMP2		EFEMP2	human	49,403							
mutant p53 binding protein 1		Q9WVJ9	mouse	49,425	Y-p						
E124		E124	human	38,065							
tumor protein p53 inducible protein 8		Q61070	mouse	38,033	K-ub, S-p, T-p						
		Q4KHK7	rat	38,093							
ENCL		ENCL	human	66,130							
tumor protein p53 inducible protein 10		O35709	mouse	66,113	K-ub, S-p, T-p, Y-p						
		Q2V9T0	rat	66,196							
GADD45GIP1		GADD45GIP1	human	25,384							
		Q8CR59	mouse	23,320	K-ub, S-p, T-p, Y-p						
		Q5AW22	rat	26,467							
		Q5S051	human	68,929							
IQCBI1		IQCBI1	mouse	68,734	K-m2, K-ub, S-p, T-p						
p53 and DNA damage-regulated IQ motif protein		Q8BP00	mouse								
IRSp53		IRSp53	human	60,868							
Insulin receptor substrate p53		BAIAP2	mouse	59,237	K-ac, K-ub, S-gl, S-p, T-p, Y-p						
		Q9UQB8	rat	59,183							
JMY		JMY	human	111,445							
junction mediating and regulatory protein, p53 cofactor		Q9QXM1	mouse	110,586	D-ca, K-ub, R-m2, S-p, T-p, Y-p						
LGALS7B		LGALS7	human	15,075							
		P47929	mouse	15,173	Y-p						
		O54974	rat								
LITAF		LITAF	human	17,107							
tumor protein p53 inducible protein 7		Q99732	mouse								
		P9JLJ0	rat								
MADIL1		MADIL1	human	16,946	K-ub, S-p, T-p, Y-p						
		Q9Y6D9	mouse	83,067							

## Modification Sites in Parent Protein, Orthologs, and Isoforms

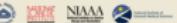
## Show Multiple Sequence Alignment

SS	MS	human		mouse		rat		rabbit		monkey	
				▼ Show Isoforms							
6	0	P4	<u>MEEPQsDpsVE</u>	S4-p	<u>MEESqSpsIle</u>	S4-p	<u>MEDsQsDMsIE</u>	S4	<u>MEESQsDLSLE</u>	P4	<u>MEEPQsDpsPSIE</u>
31	4	S6-p	<u>MEEPQsDpsVEPP</u>	S6-p	<u>MEESqSpsIleLIP</u>	S6-p	<u>MEDsQsDMsIEP</u>	S6	<u>MEESQsDLSLEPP</u>	S6	<u>MEEPQsDpsPSIEPP</u>
34	3	S9-p	<u>EKFQsDpVEPPFLQ</u>	S9-p	<u>EEQsDpIsEFLPLAQ</u>	S9-p	<u>EDsQsDmIELPLsQ</u>	S9	<u>EEQSQDLSLEPPLSQ</u>	S9	<u>EEFQsDpSIEPPFLAQ</u>
358	2	S15-p	<u>FsVEFLsQETsWDL</u>	S15-p	<u>IsELFLsQETsFGl</u>	S15-p	<u>MsIELFLsQETsCsl</u>	S15	<u>LSLEPLsQETsTSDL</u>	S15-p	<u>PSIEPPFLsQETsDSL</u>
28	0	T18-p	<u>EPFLsQETsDLWRL</u>	T18-p	<u>ELFLsQETsFaGLNL</u>	T18-p	<u>ELPLsQETsCLWRL</u>	T18	<u>EPPLsQETsDSLWRL</u>	T18	<u>EPFLsQETsTSDLWRL</u>
110	1	S28-p	<u>FLsQETsDLWLLP</u>	S28-p	<u>FLsQETsGLWLFL</u>	S28-p	<u>FLsQETsCLWLLP</u>	S28	<u>FLsQETsDSLWLLP</u>	S28	<u>FLsQETsDSLWLLP</u>
30	3	S33-p	<u>LPENHVLsTFLPsQAV</u>	P33	<u>LFFEDILsPFRCHDD</u>	P33	<u>LFPDDILsTTATGp</u>	T33	<u>LPENHVLsTFLsQAV</u>	S33-p	<u>LPENHVLsTFLsQAV</u>
65	3	S37-p	<u>NVLsPLPsQAVDQLN</u>	S34-p	<u>PFEDILsPFRCHDL</u>	S39-p	<u>LFTTATGsPHMSDl</u>	H37	<u>NLTtTSPsPFDQDL</u>	S37	<u>NVLsPLPsQAVDQLN</u>
85	2	S46-p	<u>RMDDLsLsPDDIEQW</u>	L43	<u>HCRDDLsLsPDDIEQW</u>	L48	<u>HSMDDLsLPDQVRL</u>	S45	<u>PPVDDLLsRSDVANH</u>	S46	<u>RVDDDLsSPDQLAQW</u>
15	0	T55-p	<u>DQDIEQWtEDPGFDE</u>	-	<u>qap</u>	-	<u>qap</u>	H54	<u>EDVANHsHDPPEGL</u>	T55	<u>DQDIEQWtEDPGFDE</u>
2	0	D61	<u>FEEDPGFDEAPRNPHE</u>	S55-p	<u>EEFFEGsEARLVRSG</u>	E60	<u>RELLEGsPEALVRSA</u>	E58	<u>RELLEGsPEALVRPA</u>	D61	<u>LTEDPGFDEAPRNSE</u>
8	2	T81-p	<u>RPRPAAPtPAPAPPA</u>	G75	<u>DPYETEPgPVAPAPPA</u>	A79	<u>EPGEAPAPVAPASA</u>	A78	<u>RPRPAAPtPAPAPPA</u>	T81	<u>RPRPAAPtPAPAPPA</u>
0	2	S99-p	<u>PLSSSVsQsKTYQGe</u>	S93	<u>PLSSSVsQsKTYQGe</u>	S97	<u>PLSSSVsQsKTYQGe</u>	S96	<u>PLSSSVsQsKTYQGe</u>	S99	<u>PLSSSVsQsKTYQGe</u>
1	2	K101-ub	<u>SSSVsPQsKTYQGeYG</u>	E95	<u>SSSVsPQsKTYQGeYG</u>	E99	<u>SSSVsPQsKTYQGeYG</u>	K98	<u>SSSVsPQsKTYQGeYG</u>	K101	<u>SSSVsPQsKTYQGeYG</u>
1	0	S106-p	<u>sQTYQsGyGFLGF</u>	H180	<u>sQTYQsGyGFLGF</u>	H184	<u>sQTYQsGyGFLGF</u>	H183	<u>sQTYQsGyGFLGF</u>	S106	<u>sQTYQsGyGFLGF</u>
0	1	H118-m1	<u>YQGxYGFzLsFLsLQG</u>	H184	<u>YQGxYGFzLsFLsLQG</u>	H188	<u>YQGxYGFzLsFLsLQG</u>	H187	<u>YQGxYGFzLsFLsLQG</u>	H118	<u>YQGxYGFzLsFLsLQG</u>
0	1	H115-m1	<u>GfRLsGELsGTRsKV</u>	G189	<u>GfMLGfLsGTRsKV</u>	G113	<u>GfMLGfLsGTRsKV</u>	H112	<u>GfRLGfLsGTRsKV</u>	H115	<u>GfRLGfLsGTRsKV</u>
23	1	K128-ac	<u>FLsGTRsksVtCtys</u>	K114-ac	<u>FLsGTRsksVnCtys</u>	K118-ac	<u>FLsGTRsksVnCtys</u>	K117	<u>FLsGTRsksVtCtys</u>	K128	<u>FLsGTRsksVtCtys</u>
1	19	K128-ub	<u>FLsGTRsksVnCtys</u>	K114	<u>FLsGTRsksVnCtys</u>	K118	<u>FLsGTRsksVnCtys</u>	K117	<u>FLsGTRsksVtCtys</u>	K128	<u>FLsGTRsksVtCtys</u>
1	0	Y126-p	<u>AKsVtCtysPFLnL</u>	Y126	<u>AKsVtCtysPFLnL</u>	Y124	<u>AKsVtCtysPFLnL</u>	Y123	<u>AKsVtCtysPFLnL</u>	Y122	<u>AKsVtCtysPFLnL</u>
1	1	K137-ub	<u>TsSPFLsKpCQLak</u>	K126	<u>TsSPFLsKpCQLak</u>	K130	<u>TsTSFLsKpCQLak</u>	K129	<u>TsSPFLsKpCQLak</u>	K132	<u>TsSPFLsKpCQLak</u>
1	0	K139-m1	<u>AMFcQLsKtCPVQLW</u>	K133	<u>KLFcQLsKtCPVQLW</u>	K137	<u>KLFcQLsKtCPVQLW</u>	K134	<u>KLFcQLsKtCPVQLW</u>	K139	<u>KLFcQLsKtCPVQLW</u>
3	1	S149-p	<u>PVQLWVsSTPPPGsR</u>	B143	<u>PVQLWVsSTPPPGsR</u>	S147	<u>PVQLWVsSTPPPGsR</u>	S146	<u>PVQLWVsSTPPPGsR</u>	S149	<u>PVQLWVsSTPPPGsR</u>
1	1	S149-g1	<u>PVQLWVsSTPPPGsR</u>	B143	<u>PVQLWVsSTPPPGsR</u>	S147	<u>PVQLWVsSTPPPGsR</u>	S146	<u>PVQLWVsSTPPPGsR</u>	S149	<u>PVQLWVsSTPPPGsR</u>
4	8	T158-p	<u>VQLWVsSTPPPGsR</u>	T144	<u>VQLWVsSTPPPGsR</u>	T148	<u>VQLWVsSTPPPGsR</u>	T147	<u>VQLWVsSTPPPGsR</u>	T158	<u>VQLWVsSTPPPGsR</u>
4	1	T155-p	<u>SATPPFGsVRhAII</u>	S149-p	<u>SATPPFGsVRhAII</u>	T153	<u>TSTPPFGsVRhAII</u>	T152	<u>DSTPPFGsVRhAII</u>	S155	<u>DSTPPFGsVRhAII</u>
4	1	K164-ac	<u>VRhAIIYsQsQhnte</u>	K158	<u>VRhAIIYsQsQhnte</u>	K162	<u>VRhAIIYsQsQhnte</u>	K163	<u>VRhAIIYsQsQhnte</u>	K164	<u>VRhAIIYsQsQhnte</u>
1	1	K164-ub	<u>VRhAIIYsQsQhnte</u>	K158	<u>VRhAIIYsQsQhnte</u>	K162	<u>VRhAIIYsQsQhnte</u>	K161	<u>VRhAIIYsQsQhnte</u>	K164	<u>VRhAIIYsQsQhnte</u>
2	0	S183-p	<u>CPhHERCsDSDGLAF</u>	S177	<u>CPhHERCsDSDGLAF</u>	S181	<u>CPhHERCsDSDGLAF</u>	S180	<u>CPhHERCsDSDGLAF</u>	S183	<u>CPhHERCsDSDGLAF</u>
0	1	R209-m1	<u>RVEYLDDsHtFvNsV</u>	R203	<u>RVEYLDDsHtFvNsV</u>	R207	<u>RAYELDDsHtFvNsV</u>	R206	<u>RAYELDDsHtFvNsV</u>	R209	<u>RVEYLDDsHtFvNsV</u>
1	0	T211-p	<u>EXLDsHtFvNsVV</u>	T205	<u>EXLDsHtFvNsVV</u>	T209	<u>EXLDsHtFvNsVV</u>	T208	<u>EXLDsHtFvNsVV</u>	T211	<u>EXLDsHtFvNsVV</u>
0	1	R213-m1	<u>LDsHtFvNsVVVp</u>	R207	<u>LDsHtFvNsVVVp</u>	R211	<u>LDsHtFvNsVVVp</u>	R210	<u>LDsHtFvNsVVVp</u>	R213	<u>LDsHtFvNsVVVp</u>
4	0	S225-p	<u>DrHtFvNsVVVpEp</u>	S209	<u>DrHtFvNsVVVpEp</u>	S213	<u>DrHtFvNsVVVpEp</u>	S212	<u>DrHtFvNsVVVpEp</u>	S215	<u>DrHtFvNsVVVpEp</u>



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**p53 (human)****Overview**

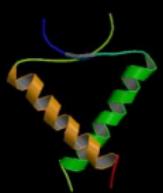
**p53** is a transcription factor and major tumor suppressor that plays a major role in regulating cellular responses to DNA damage and other genomic aberrations. Activation of p53 can lead to either cell cycle arrest and DNA repair or apoptosis. More than 50 percent of human cancers contain a mutation or deletion in the TP53 gene. p53 is modified post-translationally at multiple sites. DNA damage induces phosphorylation of p53 at S15, S20 and S37, reducing its interaction with the nucleophosmin/HDM2. HDM2 inhibits p53 accumulation by targeting it for ubiquitination and proteasomal degradation. Phosphorylated by many kinases including Chk2 and Chk1 at S20, enhancing its tetramerization, stability and activity. The phosphorylation by CK2 at S192 is increased in human tumors and has been reported to influence the growth suppressor function, DNA binding and transcriptional activation of p53. Phosphorylation of p53 at S46 regulates the ability of p53 to induce apoptosis. The acetylation of p53 appears to play a positive role in the accumulation of p53 during the stress response. Following DNA damage, p53 becomes acetylated at K382, enhancing its binding to DNA. Deacetylation of p53 can occur through interaction with SIRT1, a deacetylase that may be involved in cellular aging and the DNA damage response. p53 regulates the transcription of a set of genes encoding endosomal proteins that regulate endosomal functions. These include STEAP3 and CHMP4C, which enhance exosome production, and CAV1 and CHMP4C, which produce a more rapid endosomal clearance of the EGFR from the plasma membrane. DNA damage regulates a p53-mediated secretory pathway, involving the expression of some proteins such as Hsp90, SEC61, SEC63, MKEF-A, and vAP-2, and inhibiting the secretion of others including CTSL and IGFBP-2. Two alternatively spliced human isoforms have been reported. Isoform 2 is expressed in quiescent lymphocytes. Seems to be non-functional. May be produced at very low levels due to a premature stop codon in the mRNA, leading to nonsense-mediated mRNA Decay. Note: This description may include information from UniProtKB.

**Protein type:** DNA binding protein; Nuclear receptor co-regulator; Motility/polarity/chemotaxis; Transcription factor; Activator protein; Tumor suppressor

**Cellular Component:** PML body; transcription factor TFIID complex; protein complex; nuclear matrix; mitochondrion; endoplasmic reticulum; replication fork; cytosol; nucleoplasm; nuclear body; mitochondrial matrix; cytoplasm; nuclear chromatin; nucleolus; chromatin; nucleus

**Molecular Function:** identical protein binding; protease binding; zinc ion binding; protein phosphatase 2A binding; p53 class mediator binding; receptor tyrosine kinase binding; transcription factor activity; protein phosphatase binding; protein kinase binding; histone deacetyltransferase binding; protein binding; copper ion binding; histone deacetylase regulator activity; enzyme binding; DNA binding; protein heterodimerization activity; chaperone binding; ubiquitin protein ligase binding; damaged DNA binding; chromatin binding; transcription factor activity; ATP binding

**Biological Process:** central nervous system development; viral reproduction; positive regulation of apoptosis; multicellular organismal development; positive regulation of transcription, DNA-dependent; T cell differentiation in the thymus; gastrulation; determination of adult life span; DNA damage response; signal transduction by p53 class mediator resulting in cell cycle arrest; response to antibiotic; regulation of apoptosis; cellular response to glucose starvation; protein localization; negative regulation of neuroblast proliferation; base-excision repair; transforming growth factor beta receptor signaling pathway; protein complex assembly; cell cycle arrest; ER overload response; response to X-ray; somatogenesis; release of cytochrome c from mitochondria; chromatin assembly; cell aging; rRNA transcription; positive regulation of peptide-tyrosine phosphorylation; negative regulation of DNA replication; negative regulation of fibroblast proliferation; embryonic organ development; positive regulation of transcription from RNA polymerase II promoter; regulation of mitochondrial membrane permeability; negative regulation of transcription, DNA-dependent; regulation of tissue remodeling; negative regulation of apoptosis; G1 DNA damage checkpoint; DNA damage response; signal transduction by p53 class mediator; apoptosis; negative regulation of transcription from RNA polymerase II promoter; T cell proliferation; cell cycle arrest; negative regulation of cell proliferation; positive regulation of protein oligomerization; positive regulation of histone deacetylation; DNA damage response; signal transduction by p53 class mediator resulting in transcription of p21 class mediator; regulation of transcription, DNA-dependent; T cell proliferation during immune response; double-strand break repair; positive regulation of neuron apoptosis; response to gamma radiation; cell differentiation; DNA damage response; signal transduction by p53 class mediator resulting in induction of apoptosis; protein tetramerization; Notch signaling pathway; in utero embryonic development; multicellular organism growth; B cell lineage commitment; cell proliferation; neuron apoptosis; T cell lineage commitment; negative regulation of helicase activity; nucleotide-excision repair; protein import into nucleus; translocation; DNA strand renaturation; Ras protein signal transduction;

**Select Structure to View Below****p53**

TATU - A/C=324-356 (human)

Open Viewer

QUESTIONS?

A hand is shown writing a complex mathematical expression on a chalkboard. The expression involves terms like  $3a(y+1)^2$ ,  $(y+4)(x+1)$ , and  $a^2(y+1)^3 + \frac{2}{3}(y+4)^2(x+1)$ . Below the main term, the number 39 is written.

$$\begin{aligned} & \cancel{3a(y+1)^2} + (y+4)(x+1) \\ & \cancel{a^2(y+1)^3} + \frac{2}{3}(y+4)^2(x+1) \\ & 39 \end{aligned}$$

## CURIOSITY

"For every answer, there are but two more questions."

[motifake.com](http://motifake.com)

## The Eukaryotic Linear Motif resource for *Functional Sites in Proteins*

### The resource

is a collection of more than 240 thoroughly annotated motif classes with over 2700 annotated instances.

It is also a prediction tool to detect these motifs in protein sequences employing different filters to distinguish between **functional** and **non-functional** motif instances.

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### The resource

is a collection of more than 240 thoroughly annotated motif classes with over 2700 annotated instances.

It is also a prediction tool to detect these motifs in protein sequences employing different filters to distinguish between **functional** and **non-functional** motif instances.

Functional Sites	ELM classes	ELM instances	PDB structures	GO terms	PubMed Links
Total	155	242	2675	347	495
By category					
LIG	133	Human	1583		
MOD	31	Mouse	252	Biological Process	256
DEG	25	Rat	129		From ELM class
DOC	22	Yeast	94	Cell Compartment	112
TRG	20	Fly	90		From instance
CLV	11	Other	547	Molecular Function	127

## ELM Class

Condensed information about a motif. Regular Expressions used to annotate the motif (eg. "[KR]xLx{0,1}[FYLIVMP]" for Cyclin motif)

**DOC\_CYCLIN\_1**

**Functional site class:** Cyclin recognition site  
**Functional site description:** Functional site that interacts with cyclins, and thereby increases the specificity of phosphorylation by cyclin/CDK complexes.  
**ELM with this motif:** #DOC\_CYCLIN\_1  
**Description:** Substrate recognition site that interacts with cyclin and thereby increases phosphorylation by cyclin/cdk complexes. Predicted proteins should have a CDK phosphorylation site (#MOD\_CDCK\_4). Also used by cyclin/cdk inhibitors.  
**Pattern:** [KR].L.([0,1])[FYLIVMP]  
**Pattern Probability:** 0.0053239  
**Present in taxon:** Eukaryota  
**Interaction Domain:** Cyclin\_N (PF000134) Cyclin, N-terminal domain (Stoichiometry: 1 : 1)  
**PDB Structure:** 1Hta4 

## ELM Class

Condensed information about a motif. Regular Expressions used to annotate the motif (eg.  
”[KR]xLx{0,1}[FYLIVMP] for Cyclin motif)

■ 24 instances for DOC\_CYCLIN\_1  
(click table headers for sorting; Notes column: ▲=Number of Switches, ▼=Number of Interactions)

Protein Name	Gene Name	Start	End	Subsequence	Logic	#Ev.	Organism	Notes
JRB_HUMAN	JRB1	873	877	DRPFYRFLKLLPTEQDDEA	TP	3	Homo sapiens (Human)	1H25 ▲
JQUWJ8_CHICK	CDH1-A	394	398	RLDQESEVFLPLAMHPDPR	FP	1	Gallus gallus (Chicken)	
JPMYTL_HUMAN	JPMYTL	486	489	DPFPEFPLSLLPLPTEP	TP	1	Homo sapiens (Human)	
JEF21_HUMAN	JEF21	90	94	LDFPFYRFLKLLPTEQDDEA	TP	3	Homo sapiens (Human)	1H24
JCONIC_HUMAN	JCONIC	31	34	VLDPTEKFLPLPTEQDDEA	TP	1	Homo sapiens (Human)	
JRUX_DROME	Jrux	248	251	PTEAEKAVFLPLPTEQDDEA	TP	1	Drosophila melanogaster (Fruit Fly)	
JEF22_HUMAN	JEF22	87	91	AQELPAPFLPLPTEQDDEA	TP	1	Homo sapiens (Human)	
JEF23_HUMAN	JEF23	134	138	QDPPAFPLFLPLPTEQDDEA	TP	1	Homo sapiens (Human)	
JAKA12_MOUSE	Jakap12	501	504	EVPPDPEKFLPLPTEQDDEA	TP	1	Mus musculus (House mouse)	1▲
JCDC6_HUMAN	JCDC6	94	98	HEETLAEKFLPLPTEQDDEA	TP	2	Homo sapiens (Human)	2CCH ▲
JCON1A_HUMAN	JCON1A	19	22	HPCSKRAFLPLPTEQDDEA	TP	4	Homo sapiens (Human)	1▼ ▲
JCON1A_HUMAN	JCON1A	155	159	KHSTPFPKPLFLPLPTEQDDEA	TN	1	Homo sapiens (Human)	
JORCS6_YEAST	JORCS6	178	182	SPPPTPFLPLPTEQDDEA	TP	1	Saccharomyces cerevisiae (Baker's yeast)	
JPS3_HUMAN	JTP53	381	385	QDPPFRKFLPLPTEQDDEA	TP	5	Homo sapiens (Human)	1H26
JRBL1_HUMAN	JRBL1	658	661	DPNSKEAKFLPLPTEQDDEA	TP	3	Homo sapiens (Human)	1H28
JRBL2_HUMAN	JRBL2	680	684	PPAPTTTFLPLPTEQDDEA	TP	1	Homo sapiens (Human)	
JHRA_HUMAN	JHRA	629	633	KAASLAWKFLPLPTEQDDEA	TP	1	Homo sapiens (Human)	

### DOC\_CYCLIN\_1

Functional site class: Cyclin recognition site

Functional site description: Functional site that interacts with cyclins, and thereby increases the specificity of phosphorylation by cyclin/CDK complexes.

ELM with this model: ■DOC\_CYCLIN\_1

Description:

Substrate recognition site that interacts with cyclin and thereby increases phosphorylation by cyclin/cdk complexes. Predicted protein should have a CDK phosphorylation site (■MOD\_CDk\_4). Also used by cyclin/cdk inhibitors.

Pattern:

{[RK]} . {0,1} [FYLLVMP]

0.0053239

Present in taxon: ■Eukaryota

Interaction Domain: ■ Cyclin\_N (PF001934) Cyclin, N-terminal domain (Stoichiometry: 1 : 1)

PDB Structure: 1Hta4



## ELM Instance

An experimentally verified instance of an ELM class in a particular sequence.

## ELM Class

Condensed information about a motif. Regular Expressions used to annotate the motif (eg. "[KR]xLx{0,1}[FYLIVMP] for Cyclin motif)

### Instance

Sequence	Start	End	Subsequence	Logic	PDB	Organism	Length
...Q99741 CDCB_HUMAN	94	98	HEEILVLRKQYCDKQIQLRS	TP		Homo sapiens (Human)	560

### Instance evidence

Evidence class	PSMI	Method	BioSource	PubMed	Logic	Reliability	Notes
experimental	M60114	x-ray crystallography	In vitro	Cheng,2006	support	certain	InteractionDetection FeatureDetection
experimental	M60096	pull down	In vivo/In vitro	Petersen,1999	support	certain	InteractionDetection

This ELM instance is part of the following switching mechanism(s) annotated at the [ASwifts:ELM](#) resource:



## DOC\_CYCLIN\_1

Functional site class: Cyclin recognition site

Functional site description: Functional site that interacts with cyclins, and thereby increases the specificity of phosphorylation by cyclin/CDK complexes.

ELM with this model: #DOC\_CYCLIN\_1

Description:

Substrate recognition site that interacts with cyclin and thereby increases phosphorylation by cyclin/cdk complexes. Predicted protein should have a CDK phosphorylation site (#MOD\_CDk\_4). Also used by cyclin/cdk inhibitors.

Pattern:

[KR] . L . [D,E] [FYLIVMP]

0.0053239

Present in taxon: Eukaryota

Interaction Domain: Cyclin\_N (PF000134) Cyclin, N-terminal domain (Stoichiometry: 1 : 1)

PDB Structure: 1Hta4



## ELM Instance

An experimentally verified instance of an ELM class in a particular sequence.

- Experimental Evidences
- Methods
- References
- Interactions

## ELM Class

Condensed information about a motif. Regular Expressions used to annotate the motif (eg. "[KR]xLx{0,1}[FYLIVMP] for Cyclin motif)

### Instance

Sequence	Start	End	Subsequence	Logic	PDB	Organism	Length
...Q99741 CDCB_HUMAN	94	98	HEEILVLRKQYCDKQIQLRS	TP	2CCH	Homo sapiens (Human)	560

### Instance evidence

Evidence class	PSMI	Method	BioSource	PubMed	Logic	Reliability	Notes
experimental	M60114	x-ray crystallography	In vitro	Cheng,2006	support	certain	InteractionDetection FeatureDetection
experimental	M60096	pull down	In vivo/In vitro	Petersen,1999	support	certain	InteractionDetection

This ELM instance is part of the following switching mechanism(s) annotated at the [Δswitches.ELM](#) resource:



## DOC\_CYCLIN\_1

**Functional site class:** Cyclin recognition site  
**Functional site description:** Functional site that interacts with cyclins, and thereby increases the specificity of phosphorylation by cyclin/CDK complexes.  
**ELM with this model:** [#DOC\\_CYCLIN\\_1](#)  
**Description:** Substrate recognition site that interacts with cyclin and thereby increases phosphorylation by cyclin/cdk complexes. Predicted proteins should have a CDK phosphorylation site ([MOD\\_CDk\\_N](#)). Also used by cyclin/cdk inhibitors.  
**Pattern:** [KR] . L . [D,E] [FYLLVMP]  
**Pattern Probability:** 0.0053239  
**Present in taxon:** Eukaryota  
**Interaction Domain:** Cyclin\_N (PF000134) Cyclin, N-terminal domain (Stoichiometry: 1 : 1)  
**PDB Structure:** [1Hta4](#)



## ELM Instance

An experimentally verified instance of an ELM class in a particular sequence.

### Experimental Evidences

- Methods
- References
- Interactions

## ELM Class

Condensed information about a motif. Regular Expressions used to annotate the motif (eg. "[KR]xLx{0,1}[FYLIVMP] for Cyclin motif)

### Instance

Sequence	Start	End	Subsequence	Logic	PDB	Organism	Length
...Q99741 CDCB_HUMAN	94	98	HEEILVLRQYVCDKQTLRS	TP	2CCH	Homo sapiens (Human)	560

### Instance evidence

Evidence class	PSMI	Method	BioSource	PubMed	Logic	Reliability	Notes
experimental	M61014	x-ray crystallography	In vitro	Cheng,2006	support	certain	InteractionDetection FeatureDetection
experimental	M61096	pull down	In vivo/In vitro	Petersen,1999	support	certain	InteractionDetection

This ELM instance is part of the following switching mechanism(s) annotated at the [Δswitches.ELM](#) resource:



## DOC\_CYCLIN\_1

Functional site class: Cyclin recognition site

Functional site description: Functional site that interacts with cyclins, and thereby increases the specificity of phosphorylation by cyclin/CDK complexes.

ELM with this model: #DOC\_CYCLIN\_1

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Substrate recognition site that interacts with cyclin and thereby increases phosphorylation by cyclin/cdk complexes. Predicted protein should have a CDK phosphorylation site (#MOD\_CDCK\_4). Also used by cyclin/cdk inhibitors.

Pattern:

[KR] . L . [D,E] [FYLLVRF]

0.0053239

Present in taxon: Eukaryota

Interaction Domain: Cyclin\_N (PF000134) Cyclin, N-terminal domain (Stoichiometry: 1 : 1)

PDB Structure: 1ITa4



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### Instance evidence

Evidence class	PSMI	Method	BioSource	PubMed	Logic	Reliability	Notes
experimental	M61014	x-ray crystallography	In vitro	Cheng,2006	support	certain	InteractionDetection FeatureDetection
experimental	M61006	pull down	In vivo/In vitro	Petersen,1999	support	certain	InteractionDetection

This ELM instance is part of the following switching mechanism(s) annotated at the [Δswitches.ELM](#) resource:



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Functional site class: Cyclin recognition site

Functional site description: Functional site that interacts with cyclins, and thereby increases the specificity of phosphorylation by cyclin/CDK complexes.

ELM with this model: #DOC\_CYCLIN\_1

Description:

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Pattern:

[KR] . L . [D,E] [FYLIVMP]

0.0053239

Present in taxon: Eukaryota

Interaction Domain: Cyclin\_N (PF000134) Cyclin, N-terminal domain (Stoichiometry: 1 : 1)

PDB Structure: 1Hta4



## ELM Instance

An experimentally verified instance of an ELM class in a particular sequence.

- Experimental Evidences
- Methods
- References
- Interactions

## ELM Class

Condensed information about a motif. Regular Expressions used to annotate the motif (eg. "[KR]xLx{0,1}[FYLIVMP] for Cyclin motif)

### Instance

Sequence	Start	End	Subsequence	Logic	PDB	Organism	Length
...Q99741 CDCB_HUMAN	94	98	HEEILAEKQYVCDKQIQLRS	TP		Homo sapiens (Human)	560

### Instance evidence

Evidence class	PBM	Method	BioSource	PubMed	Logic	Reliability	Notes
experimental	MI0114	x-ray crystallography	In vitro	Cheng,2006	support	certain	InteractionDetection FeatureDetection
experimental	MI0096	pull down	In vivo/In vitro	Petersen,1999	support	certain	InteractionDetection

This ELM instance is part of the following switching mechanism(s) annotated at the [ASwifts:ELM](#) resource:



## DOC\_CYCLIN\_1

Functional site class: Cyclin recognition site

Functional site description: Functional site that interacts with cyclins, and thereby increases the specificity of phosphorylation by cyclin/CDK complexes.

ELM with this model: #DOC\_CYCLIN\_1

Description:

Substrate recognition site that interacts with cyclin and thereby increases phosphorylation by cyclin/cdk complexes. Predicted protein should have a CDK phosphorylation site (#MOD\_CDCK\_4). Also used by cyclin/cdk inhibitors.

Pattern:

[KR] . L . [D,I] [FYLLIVRP]

0.0053239

Present in taxon: Eukaryota

Interaction Domain: Cyclin\_N (PF000134) Cyclin, N-terminal domain (Stoichiometry: 1 : 1)

PDB Structure: [1H24](#)



## ELM Instance

An experimentally verified instance of an ELM class in a particular sequence.

- Experimental Evidences
- Methods
- References
- Interactions



## The Eukaryotic Linear Motif resource for Functional Sites in Proteins

[ELM Home](#) [ELM Prediction](#) [ELM DB](#) [ELM Candidates](#) [ELM](#)

[ELM classes](#)

[ELM instances](#)

[ELM pdb structures](#)

[ELM binding domains](#)

### SEARCH the ELM

The ELM relational database is curated from the literature. The site contains one to many ELM validated motif instances matching the website according to the following:

239 annotated [ELM classes](#)

2,675 experimentally validated [ELM viral instances](#)

100 [ELM methods](#) described

358 solved [PDB structures](#)

118 globular [ELM binders](#)

1,031 [interactions](#) mediated by 25

836 regulatory [switches](#) mediated by curated ELM instances (from [Switches.ELM DB](#))

784 [pathways](#) from [KEGG](#) involving linear motifs annotated in 832 Sequences

219 [viral instances](#) interfering with host cellular processes

11 [ELM related diseases](#) annotated as being caused by aberrant motif function

2 examples where [pathogens abuse](#) motifs to deregulate host cells

Search ELM Instances and Classes

search ELM Database

kelch

ELM CLASS: DEG\_Kelch\_actinfilin\_1

ELM CLASS: DEG\_Kelch\_Keap1\_1

ELM CLASS: DEG\_Kelch\_Keap1\_2

ELM CLASS: DEG\_Kelch\_KLHL3\_1

INSTANCE: P42260 GRK2\_RAT [881:885] DEG\_Kelch\_actinfilin\_1

INSTANCE: Q14494 NF2L1\_HUMAN [231:236] DEG\_Kelch\_Keap1\_1

INSTANCE: Q16236 NF2L2\_HUMAN [77:82] DEG\_Kelch\_Keap1\_1

INSTANCE: P20482 CNC\_DROME [458:463] DEG\_Kelch\_Keap1\_1

INSTANCE: Q13501 SQSTM\_HUMAN [347:352] DEG\_Kelch\_Keap1\_1

INSTANCE: Q96HS1-1 PGAMS\_HUMAN [77:82] DEG\_Kelch\_Keap1\_1

INSTANCE: O14920 IKKB\_HUMAN [34:39] DEG\_Kelch\_Keap1\_1

INSTANCE: Q5JTC6 AMER1\_HUMAN [286:291] DEG\_Kelch\_Keap1\_1

INSTANCE: Q86YC2 PALB2\_HUMAN [89:94] DEG\_Kelch\_Keap1\_1

INSTANCE: Q13402 MYO7A\_HUMAN [1636:1641] DEG\_Kelch\_Keap1\_1

INSTANCE: Q12830 BPTF\_HUMAN [729:734] DEG\_Kelch\_Keap1\_1

■ DEG\_SPOP\_SBC\_1,

■ DOC\_GSK3\_Axin\_1,

■ LIG\_CID\_NIM\_1,

■ LIG\_GBD\_WASP\_1,

■ LIG\_Mtr4\_Air2\_1,

■ LIG\_Mtr4\_Trf4\_1,

■ LIG\_Mtr4\_Trf4\_2,

■ LIG\_Pex14\_3,

■ LIG\_Pex14\_4,

■ LIG\_RPA\_C\_Funaf,

■ LIG\_RPA\_C\_Insects,

■ LIG\_RPA\_C\_Plants,

■ LIG\_RPA\_C\_Vert,

■ MOD\_SUMO\_rev\_2


 search ELM Database

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[Help](#)
[«MOD\\_WntLipid»](#)
[»TRG\\_Cilium\\_Arf4\\_1«](#)

## TRG\_AP2beta\_CARGO\_1

**Accession:** [ELME000247](#)

**Functional site class:** AP-2 beta2 appendage CCV component motifs

**Functional site description:** Several motifs are responsible for the binding of accessory endocytic proteins to the beta2-subunit appendage of the adaptor protein complex AP-2 as part of their recruitment to the site of clathrin coated vesicle (CCV) formation. Proteins binding the platform subdomain have been found to be cargo family specific (for example can load all GPCRs, or all LDL receptor family members) clathrin adaptors. Accessory proteins which help in CCV formation bind the sandwich subdomain site or the alpha ear domain.

**ELM Description:** Motif binding as a helix in a depression on the top surface of the AP-2 beta appendage platform subdomain. The pattern [ED]x{1,2}Fxx[FL]xxxR is conserved in beta Arrestins, ARH and Epsin-1, -2 of vertebrates. It is also found in homologues of other metazoans, but the pattern is sometimes not matched exactly, meaning that the ELM regular expression will not provide a match. In other lineages, if there is an equivalent motif, the pattern is likely to have diverged.

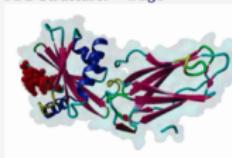
**Pattern:** [DE].{1,2}F[^P][^P][FL][^P][^P][^P]R

**Pattern Probability:** 0.0000182

**Present in taxon:** [Metazoa](#)

**Interaction Domain:** B2-adapt-app\_C (PF09066) Beta2-adaptin appendage, C-terminal sub-domain (Stoichiometry: 1 : 1)

PDB Structure: [1zG3o](#)




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## Search ELM Instances

Full-Text Search (to show all instances, enter 'all' or '')

Filter by instance Logic true positive | Filter by organism Homo sapiens

export 58 instances as: [fasta](#) | [tsv](#)

■ 58 Instances for search term 'ap2':

(click table headers for sorting)

CLV  
LIG  
MOD  
TRG

ELM identifier	Sequence	Start	End	Subsequence	Instance Logic	#Evidence	PDB	Organism
TRG_LysEnd_APsAcLL_1	OPRD_HUMAN	241	246	GLMLLRLRSVRLSGSKEKD	true positive	8	---	Homo sapiens (Human)
TRG_AP2beta_CARGO_1	ARRB1_HUMAN	385	395	TND <span style="background-color: blue;">D</span> IVFEDFARQR <span style="background-color: blue;">R</span> LKG <span style="background-color: blue;">M</span> K	true positive	5	2IV8	Homo sapiens (Human)
TRG_LysEnd_APsAcLL_1	HG2A_HUMAN	19	24	DQKPVMD <span style="background-color: blue;">Q</span> RDL <span style="background-color: blue;">I</span> SNNEQLP	true positive	5	---	Homo sapiens (Human)
LIG_AP2alpha_2	EPS15_HUMAN	672	674	DPFATSS <span style="background-color: blue;">T</span> DPFA <span style="background-color: blue;">P</span> GTVVAA	true positive	4	---	Homo sapiens (Human)
LIG_AP2alpha_2	EPS15_HUMAN	692	694	SVETLKHN <span style="background-color: blue;">D</span> PPAFPGTVVA	true positive	4	---	Homo sapiens (Human)
LIG_AP2alpha_2	EPS15_HUMAN	709	711	VAASDSAT <span style="background-color: blue;">D</span> PPFA <span style="background-color: blue;">P</span> VFGNESF	true positive	4	---	Homo sapiens (Human)
LIG_AP2alpha_2	EPS15_HUMAN	737	739	TLSKVNNE <span style="background-color: blue;">D</span> PPERSATSSVS	true positive	4	---	Homo sapiens (Human)
TRG_AP2beta_CARGO_1	EPN1_HUMAN	377	386	FDTEP <span style="background-color: blue;">D</span> EFS <span style="background-color: blue;">E</span> FD <span style="background-color: blue;">R</span> LR <span style="background-color: blue;">T</span> ALPT	true positive	4	---	Homo sapiens (Human)
TRG_LysEnd_APsAcLL_1	ATP7A_HUMAN	1483	1488	SVVTSEPA <span style="background-color: blue;">H</span> SL <span style="background-color: blue;">L</span> VGFRED	true positive	4	---	Homo sapiens (Human)
LIG_SxIP_EBH_1	CLAP2_HUMAN	492	502	ASAQ <span style="background-color: blue;">K</span> R <span style="background-color: blue;">S</span> KIPIPSQGC <span style="background-color: blue;">S</span> REAS	true positive	3	---	Homo sapiens (Human)
LIG_SxIP_EBH_1	CLAP2_HUMAN	515	525	LSVA <span style="background-color: blue;">R</span> SSRIPR <span style="background-color: blue;">P</span> SVS <span style="background-color: blue;">Q</span> CSR	true positive	3	---	Homo sapiens (Human)
TRG_LysEnd_APsAcLL_1	BCAM_HUMAN	604	609	HSGSEQPEQT <span style="background-color: blue;">G</span> LL <span style="background-color: blue;">M</span> GGASGG	true positive	3	---	Homo sapiens (Human)
TRG_LysEnd_APsAcLL_1	NPC1_HUMAN	1271	1276	KSCATEERYKG <span style="background-color: blue;">T</span> ERERLLNF	true positive	3	---	Homo sapiens (Human)
LIG_APCC_KENbox_2	CKAP2_HUMAN	80	84	KLKTKMA <span style="background-color: blue;">D</span> KEN <span style="background-color: blue;">M</span> KRAESKN	true positive	2	---	Homo sapiens (Human)
LIG_MAPK_1	MP2K1_HUMAN	3	11	MPKKKPTPIQLNPADGS <span style="background-color: blue;">A</span> V	true positive	2	---	Homo sapiens (Human)
LIG_MAPK_1	MP2K4_HUMAN	40	48	SSMQG <span style="background-color: blue;">K</span> R <span style="background-color: blue;">K</span> A <span style="background-color: blue;">L</span> KN <span style="background-color: blue;">F</span> ANPPFK	true positive	2	---	Homo sapiens (Human)
TRG_AP2beta_CARGO_1	ARH_HUMAN	256	266	DDGL <span style="background-color: blue;">D</span> EAFS <span style="background-color: blue;">R</span> LA <span style="background-color: blue;">Q</span> SRT <span style="background-color: blue;">T</span> NPQV	true positive	2	2G30	Homo sapiens (Human)
TRG_LysEnd_APsAcLL_1	CD44_HUMAN	708	713	GEASKS <span style="background-color: blue;">O</span> M <span style="background-color: blue;">H</span> VL <span style="background-color: blue;">N</span> KESSET	true positive	2	---	Homo sapiens (Human)
LIG_AP2alpha_1	AMPH_HUMAN	324	328	QENIISF <span style="background-color: blue;">F</span> EDN <span style="background-color: blue;">P</span> VPEIS <span style="background-color: blue;">V</span> TT	true positive	1	1KY7	Homo sapiens (Human)



## Diseases mediated by short linear motifs

Several diseases are known which are caused by one or more mutations in linear motifs mediating important interactions. Below you find a selection of such diseases; for linear motifs abused by viruses, see the dedicated [Viruses](#) page. For a large-scale analysis on disease-causing mutations see [\[Proteome-wide analysis of human disease mutations in short linear motifs: neglected players in cancer? Uyar B, et al., 2014\]](#)

### Noonan Syndrome

The developmental disorder "Noonan Syndrome" can be caused by mutations in [DRaf-1](#) which abrogate the interaction with 14-3-3 proteins mediated by corresponding motifs and thereby deregulate the Raf-1 kinase activity [[Pandit et al., 2007](#)]. The [DRaf-1](#) sequence features two [LIG\\_14-3-3\\_1](#) binding sites, which are annotated at [256-261](#) and [618-623](#).

### Noonan-like Syndrome

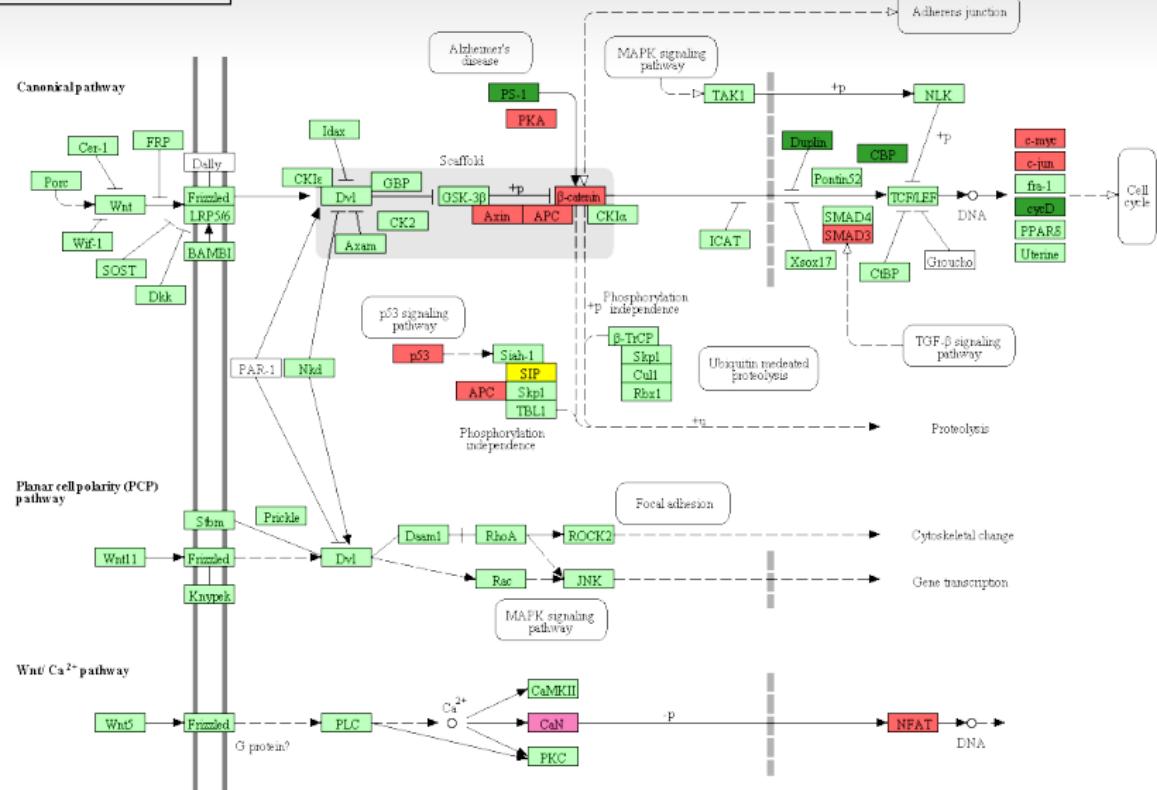
A S->G mutation at position 2 creates a novel [MOD\\_NMyristoyl](#) site (irreversible modification) resulting in aberrant targeting of SHOC2 to the plasma membrane and impaired translocation to the nucleus upon growth factor stimulation [[Cordedu et al., 2007](#)].

### Usher's Syndrome

"Usher's Syndrome" is the most frequent cause of hereditary deaf-blindness in humans [[Eudy and Sumegi, 1999](#)], affecting one child in 25 000. This disease can be caused by mutations in either PDZ domains in [Harmonin](#) or the corresponding PDZ interaction motifs in the [SANS](#) protein (annotated at [456-461](#)) [[Weil et al., 2003](#), [Kalay et al., 2005](#)].

Another example implicating PDZ domains is "*familial hypomagnesemia with hypercalciuria and nephrocalcinosis*" (FHHN), an autosomal recessive wasting disorder of renal Mg<sup>2+</sup> and Ca<sup>2+</sup> that leads to progressive kidney failure. Here, motifs mediating interaction to PDZ domains are mutated in [Claudin 16](#), abolishing important interactions to the scaffolding protein [ZO-1](#) resulting in lysosomal mislocalization of the protein [[Müller et al., 2003](#), [Müller et al., 2006](#)].

## WNT SIGNALING PATHWAY





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## Functional site prediction

### Protein sequence

Enter Uniprot identifier or accession number: (auto-completion)  
e.g. **EPN1\_HUMAN, P04637, TAU\_HUMAN, [RANDOM]**

**EPN1\_HUMAN** CRYPONETRIA PARASITICA

EPD1\_CARAU [P13506] CARASSIUS AURATUS

**EPN1\_ARATH** [Q8VY07] ARABIDOPSIS THALIANA

**EPN1\_HUMAN** [Q9Y6I3] HOMO SAPIENS

**EPN1\_MOUSE** [Q80VP1] MUS MUSCULUS

**EPN1\_RAT** [Q88339] RATTUS NORVEGICUS

F2QLC2\_PICP7 [F2QLC2] KOMAGATAELLA PASTORIS

KOKY34\_WICCF [KOKY34] WICKERHAMOMYCES CIFERRIL

A0A024R4S1\_HUMAN [A0A024R4S1] HOMO SAPIENS

K7EMP4\_HUMAN [K7EMP4] HOMO SAPIENS

W8B7F4\_CERCA [W8B7F4] CERATIS CAPITATA

A8X4H2\_CAEBR [A8X4H2] CAENORHABDITIS BRIGGSAE

Q8B1I7\_CAEEL [Q8B1I7] CAENORHABDITIS ELEGANS

Q8P7E0\_GAFEL [Q8P7E0] GAFELLA

cytosol  
peroxisome  
glycosome  
glyoxosome

(ASTA format):

```
SEIMSMNIWKRLNDHGKNWRHVYKAMTL
DLRDEDRLLRERAHALKTTEKLQAQTATA
QLALSLSLREEDKEERIRGGDDLRLQM
IDPWGGPPVPPAAADPWWGPAPTPGASGDP
FAFSDPNGGSPAKPSTNGTAAAGGFDT
ISPPTAATPTPTPPTRKTTESFLGPNA
RLSPVPPPGAPPTYISPLGGGGPLPP
```

### Taxonomic Context

Type in species name (auto-completion):

Homo sapiens

### Motif Probability Cutoff:

#### ■ ELM database update

The following elm classes have been added to the database:

- [DEG Kelch\\_actinfilin\\_1](#)
- [DEG Kelch\\_Keap1\\_1](#)
- [DEG Kelch\\_Keap1\\_2](#)
- [DEG Kelch\\_KLHL3\\_1](#)
- [DEG Nend\\_Nbox\\_1](#)
- [DEG Nend\\_UBRbox\\_1](#)
- [DEG Nend\\_UBRbox\\_2](#)
- [DEG Nend\\_UBRbox\\_3](#)
- [DEG Nend\\_UBRbox\\_4](#)
- [DEG SPOP\\_SBC\\_1](#)
- [DOC\\_GSK3\\_Axin\\_1](#)
- [LIG\\_CID\\_NIM\\_1](#)
- [LIG\\_GBD\\_WASP\\_1](#)
- [LIG\\_Mtr4\\_Air2\\_1](#)
- [LIG\\_Mtr4\\_Trf4\\_1](#)
- [LIG\\_Mtr4\\_Trf4\\_2](#)
- [LIG\\_Pex14\\_3](#)
- [LIG\\_Pex14\\_4](#)
- [LIG\\_RPA\\_C\\_Fungi](#)
- [LIG\\_RPA\\_C\\_Insects](#)
- [LIG\\_RPA\\_C\\_Plants](#)
- [LIG\\_RPA\\_C\\_Vert](#)
- [MOD\\_SUMO\\_rev\\_2](#)

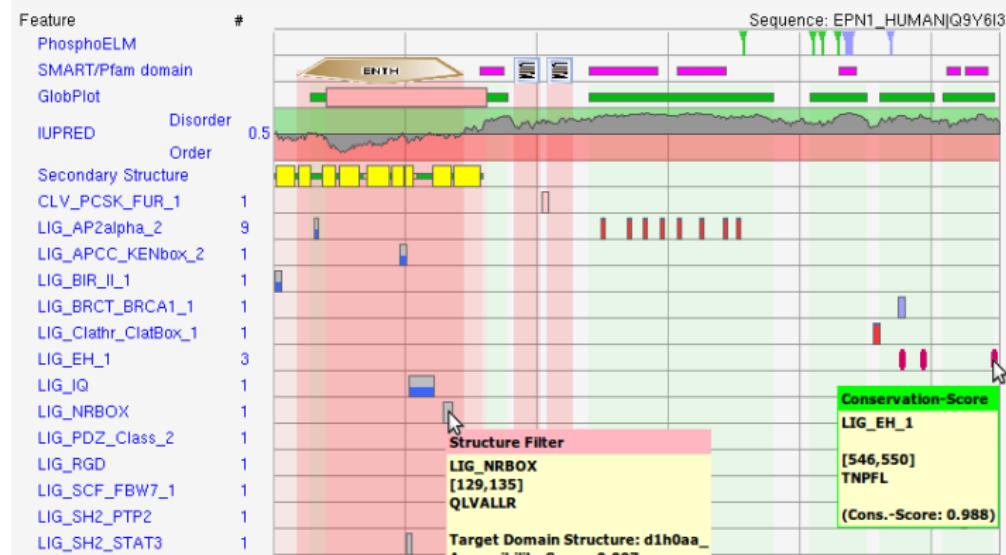
Many new instances: 8

## ■ Summary of features reported by the ELM resource.

### KEY

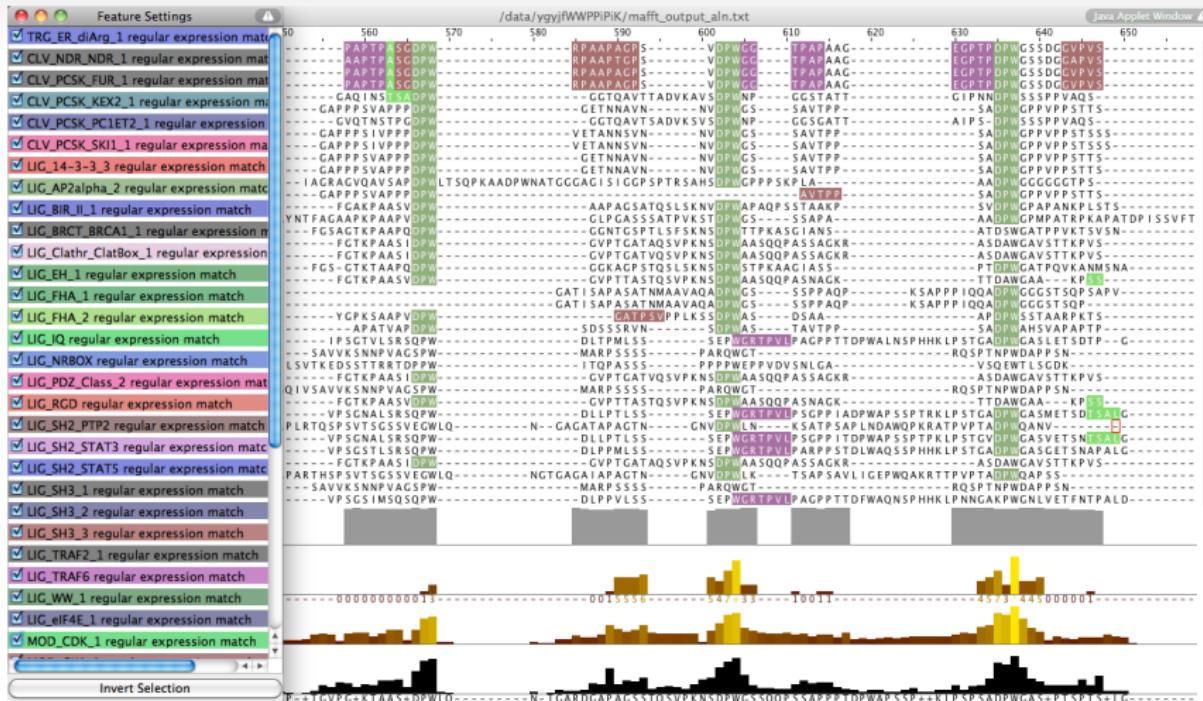
DOMAINS:	Smart/Pfam domain	Signal peptide (pred.)	Low-complexity region	Coiled-coil (pred.)	TM helix (pred.)
GLOBPLOT:	GlobDom		Disorder		
2D STRUCT:	Strand	Helix	Loop		3/10 Helix
MOTIFS:	Favourable Context	Sparse/Smart filtered	Neutral	Annotated:	TP  FP  TN  FN  <  <  Assigned by homology
CONSCORE:	low Conservation	medium Conservation	high Conservation		

(Mouseover the matches for more details )



# VIEW CONSERVATION IN JALVIEW

ELM



# Questions?



# CURIOSITY

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## Short Linear Motifs

- are compact, degenerate protein interaction interfaces (in IDRs)
- are ubiquitous in eukaryotic proteomes and mediate many regulatory functions:
  - directing ligand binding
  - providing docking sites for modifying enzymes
  - controlling protein stability
  - acting as signals to target proteins to specific subcellular locations

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## Motif-mediated interactions

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- are transient & reversible
- can be easily modulated.

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## Motif-mediated interactions

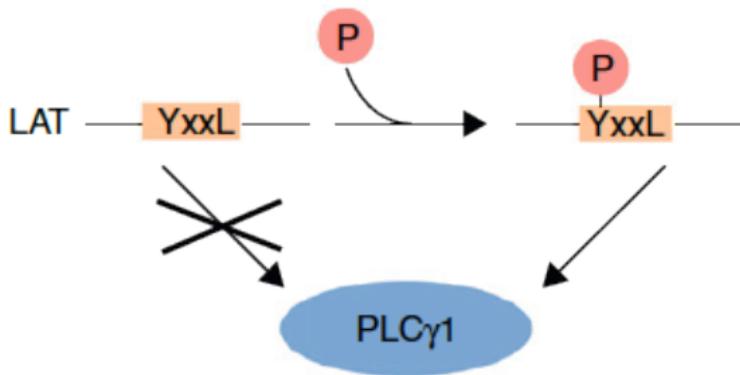
- occur with low affinity,
- are transient & reversible
- can be easily modulated.

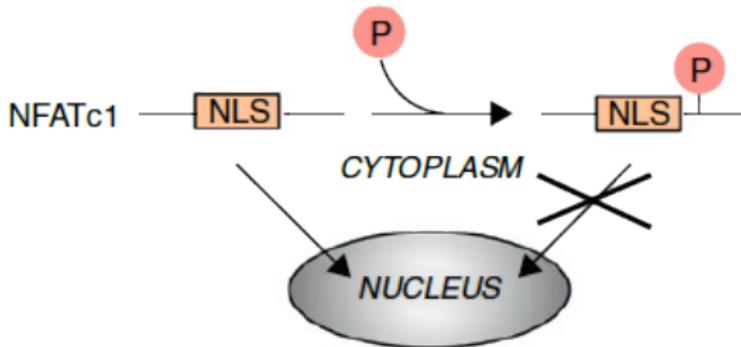
## Motifs mediate switches

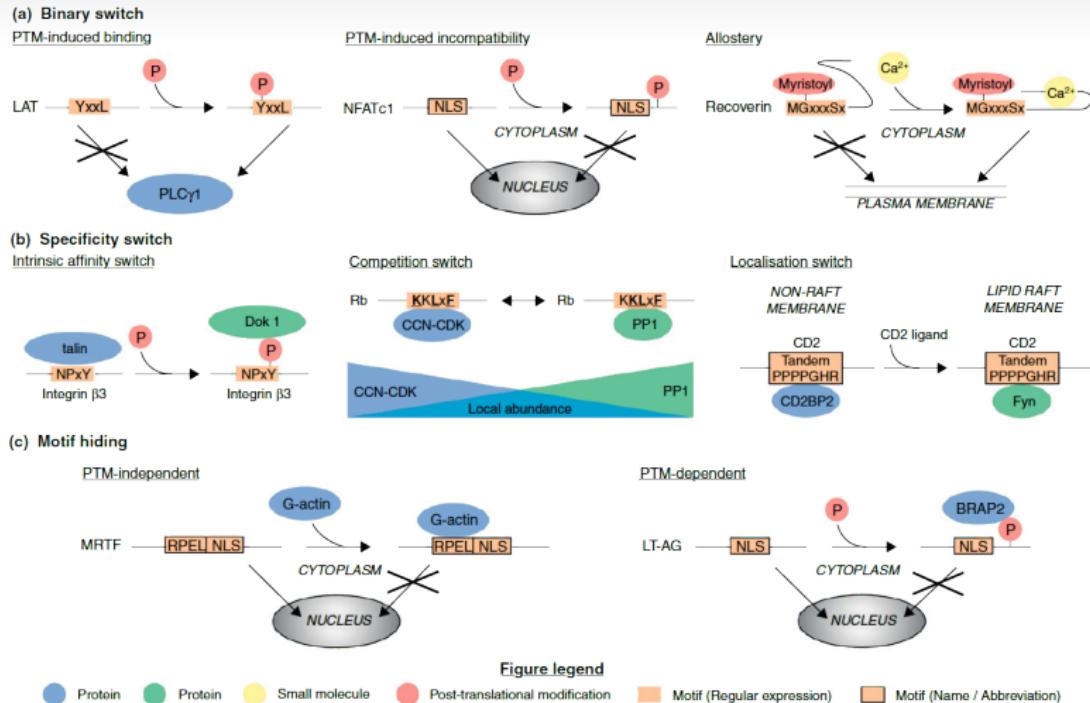
This makes SLiMs ideal regulatory modules and enable them to conditionally **switch** between “on” and “off” states or between multiple, functionally distinct on states.

*The switches.ELM Resource: A Compendium of Conditional Regulatory Interaction Interfaces*”; VAN ROEY, DINKEL, WEATHERITT, GIBSON AND DAVEY; (SCIENCE SIGNALING. 2013)

Tools & Databases of Short Linear Motifs

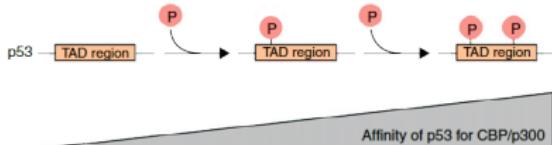
PTM-induced binding

PTM-induced incompatibility

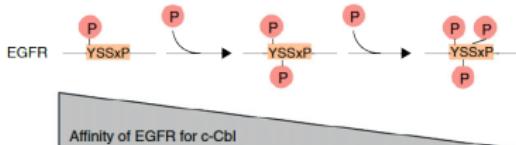


**(a) Cumulative switch**

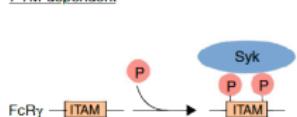
Positive rheostat



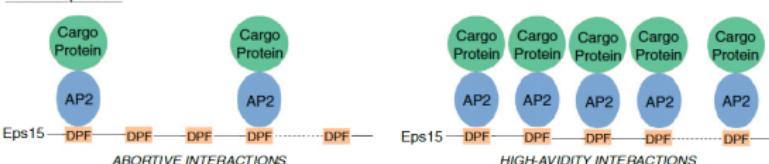
Negative rheostat

**(b) Avidity-sensing switch**

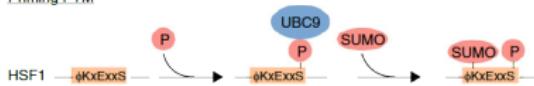
PTM-dependent



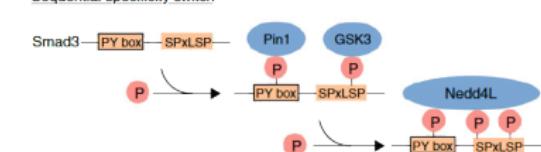
PTM-independent

**(c) Sequential switch**

Priming PTM



Sequential specificity switch

**Figure legend**

- Protein
- Protein
- Small molecule
- Post-translational modification
- Motif (Regular expression)
- Motif (Name / Abbreviation)

The switches.ELM **database** curates experimentally validated motif-based molecular switches.

In addition, based on these validated instances, the switches.ELM **prediction** tool was developed to identify possible switching mechanisms that might regulate a motif-containing protein of interest.

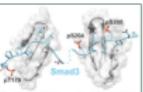
**switches.ELM**

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**Introduction**

The switches.ELM resource, hosted by the ELM consortium at the European Molecular Biology Laboratory (EMBL), consists of a database that curates experimentally validated motif-based molecular switches and a prediction tool to identify possible switching mechanisms that might regulate a user-submitted motif of interest. This tool helps to extend knowledge and direct research on how motifs mediate cooperative decision-making in a context-dependent manner and direct reliable and robust cell regulation.

**Switch of the month**



A Smad activation turnover switch operated by WW domain readers of a phosphoserine code.  
Aragon et al., Genes Dev, 2011

Links: [PubMed](#) [Genes Dev](#) [switches.ELM](#)

**Submit a paper for curation**

**Links**

[View predicted switches in the ELM database.](#)  
[View switches currently awaiting curation.](#)

**Analyse proteins for novel switches**

**Browse database by**

**Search database**

Examples: Phosphorylation | Mouse | LIG\_CYCLIN\_1

**Analyse proteins for novel switches**

Examples: P04637 | TP53 | Tumor suppressor p53






The switches.ELM **database** curates experimentally validated motif-based molecular switches.

In addition, based on these validated instances, the switches.ELM **prediction** tool was developed to identify possible switching mechanisms that might regulate a motif-containing protein of interest.

**Switch #:** SWT10000055 ◊    **Switch type:** Binary ◊    **Switch subtype:** Physicochemical compatibility ◊

**Switch Description:**  
Phosphorylation of S203 in the Pin1-binding motif of Steroidogenic factor 1 (Nr5a1) induces binding to the Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1 (Pin1) protein.

**Participants:**  
 (1) Steroidogenic factor 1 (Nr5a1)  
 (2) Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1 (Pin1)

**Interactions**

**Interaction #1 Nr5a1 - Pin1**

**Interfaces**

(1) LIG\_WW\_Pin1\_4 motif (200PYASPP205) in Steroidogenic factor 1 (Nr5a1)  
 (2) WW domain (7-37) in Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1 (Pin1)

**Interaction Regulation**

PTM-dependent induction (Phosphorylation of S203 on Steroidogenic factor 1 (Nr5a1)) of the Steroidogenic factor 1 (Nr5a1) LIG\_WW\_Pin1\_4 motif - Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1 (Pin1) WW domain interaction

**References**

(1) Pin1 facilitates the phosphorylation-dependent ubiquitination of SF-1 to regulate gonadotropin beta-subunit gene transcription.  
 Luo et al. Mol. Cell. Biol. (2010)

**See also**

Other switches involving participants

**Steroidogenic factor 1 (Nr5a1)**

Alignment	Motifs	Modification	Switches	Structure	Mutation	Isolforms	SNPs	Features	Disorder
offset	?	1182							
MOTIF of interest	?		SWAPPin1						
MOUSE (toggle extra species)	?								
BOVIN									
CHICKEN									
DRAGO									
PANTHER									
CION									
DROME									
APIME									
CAEEL									
<b>switches</b>	?		WW_Pin1						
<b>Modification switches</b>	?								
<b>ELM ( toggle predicted hits )</b>	?								
<b>ELM regex</b>	?		AMYPT1 SH2 SH3 SH2 STV CK2 ENDOCYN-GLC SUMO	PCSK SKD BIR inter CK2 SUMO	WW_Pin1 BIR inter CK2 SH3 WW_Pin1 ProDKin	MYPT1 CK2 SH3 GlnNhd			
<b>modified residue</b>	?								
phospho.ELM	?								
phosphoSitePlus	?								
<b>secondary structure (+ details)</b>	?								
<b>chain</b>	?		Steroidogenic factor 1						
<b>cross-link</b>	?								
<b>disorder</b>	?								

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# Questions?



CURIOSITY KILLED THE CAT

Good boy curiosity.....  
Good boy!!!

[motifake.com](http://motifake.com)