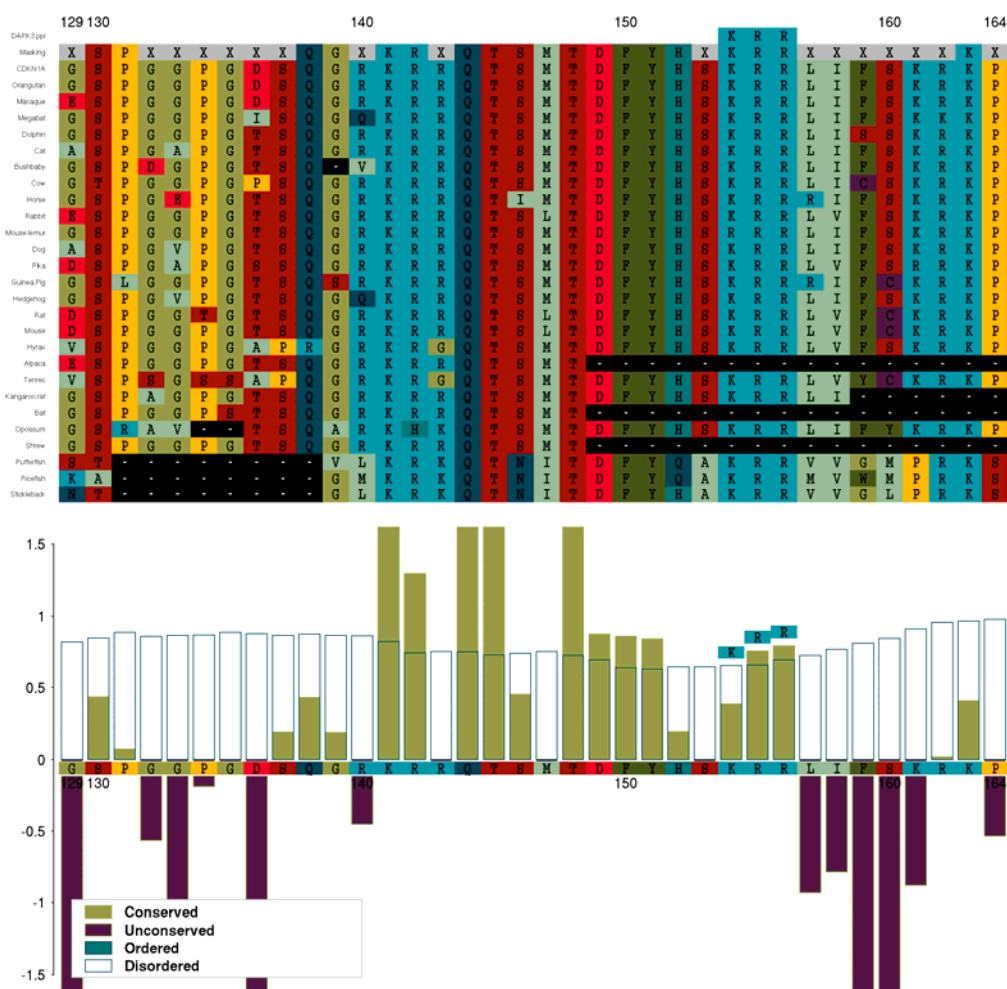
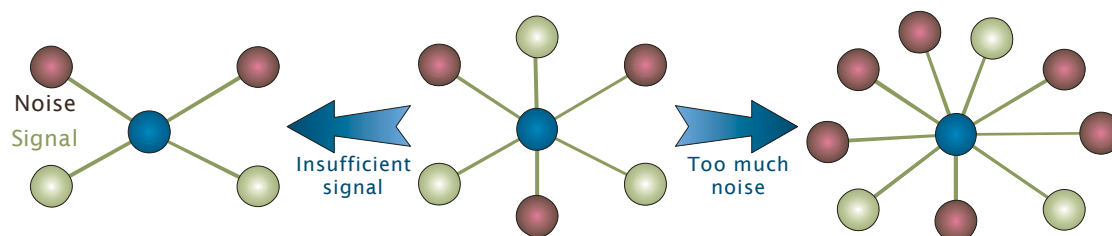


Supplementary Figures



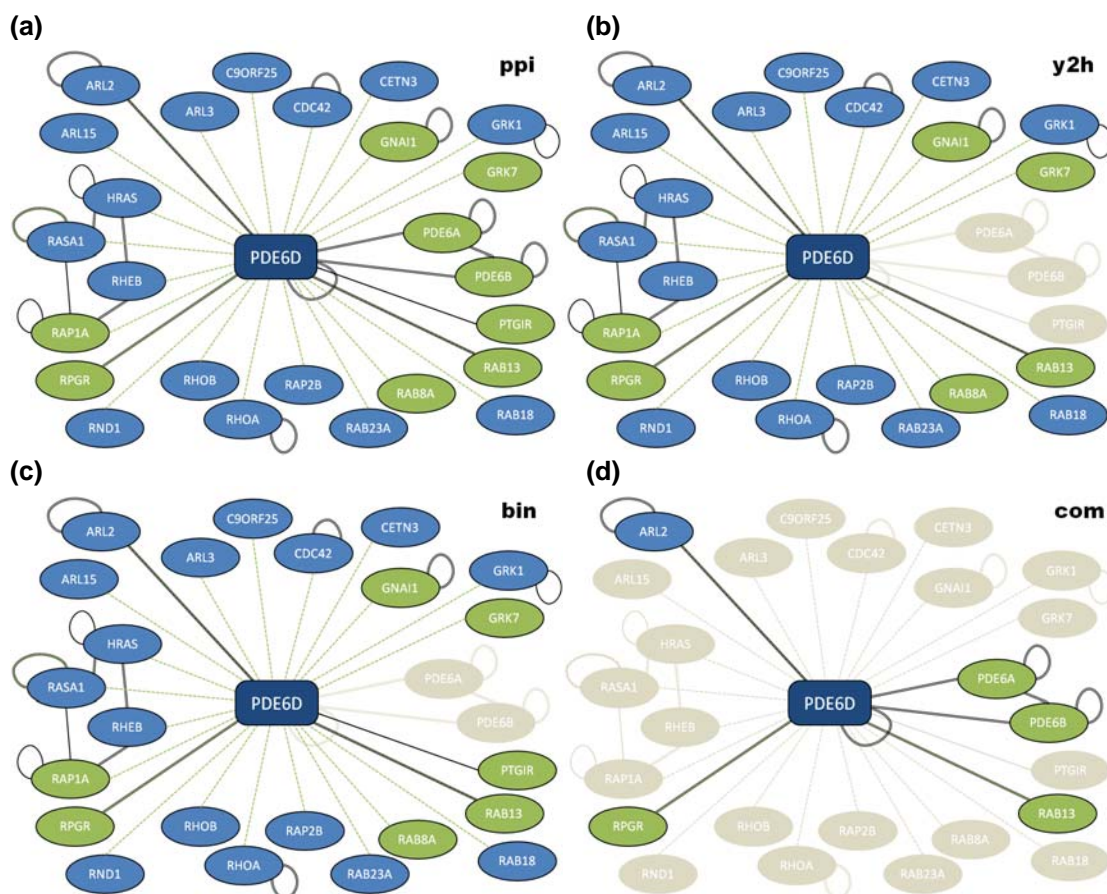
Supplementary Fig. S1. Region of CDKN1A showing conserved PCNA ligand motif.

The upper panel shows an alignment of a region of human CDKN1A with predicted vertebrate orthologues. The lower panel plots Relative Local Conservation (RLC) and IUPred disorder prediction scores for each residue. Residues designated “unconserved” (RLC < 0) and/or “disordered” (IUPred < 0.2) were masked out of the analysis (X in the “Masking” row of the alignment).



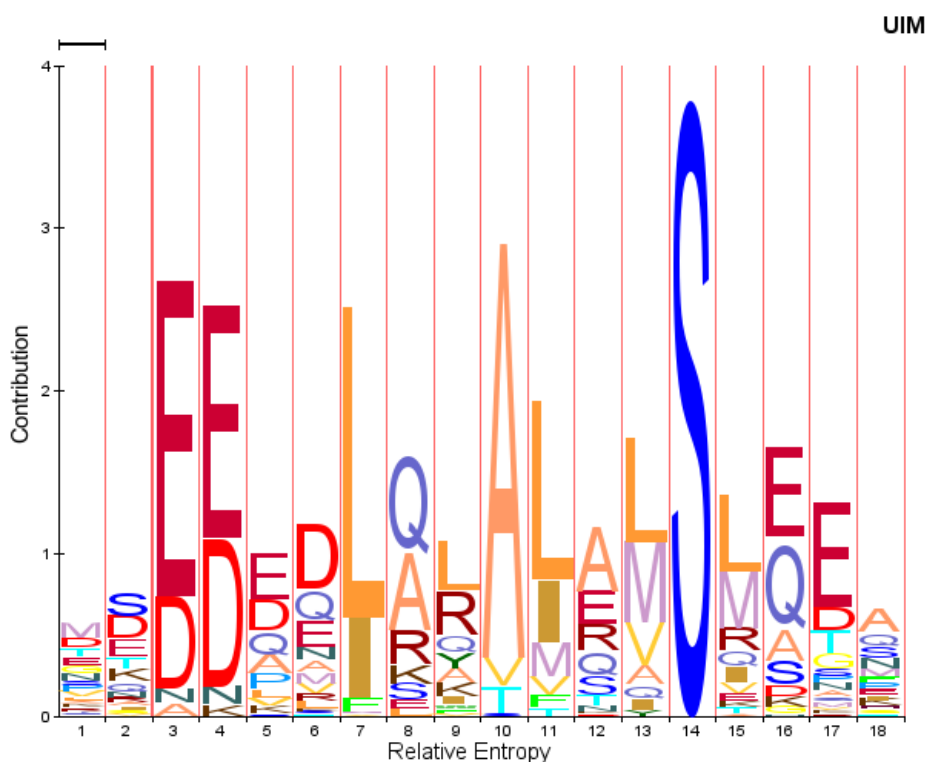
Supplementary Fig. S2. Signal-to-noise trade-off.

Dataset quality has a big impact on results quality. Adding incorrect interactors will increase the noise. Inadvertently removing correct interactors, however, will reduce the signal. There is therefore a trade-off in the strictness of selection criteria for accepted interactors.

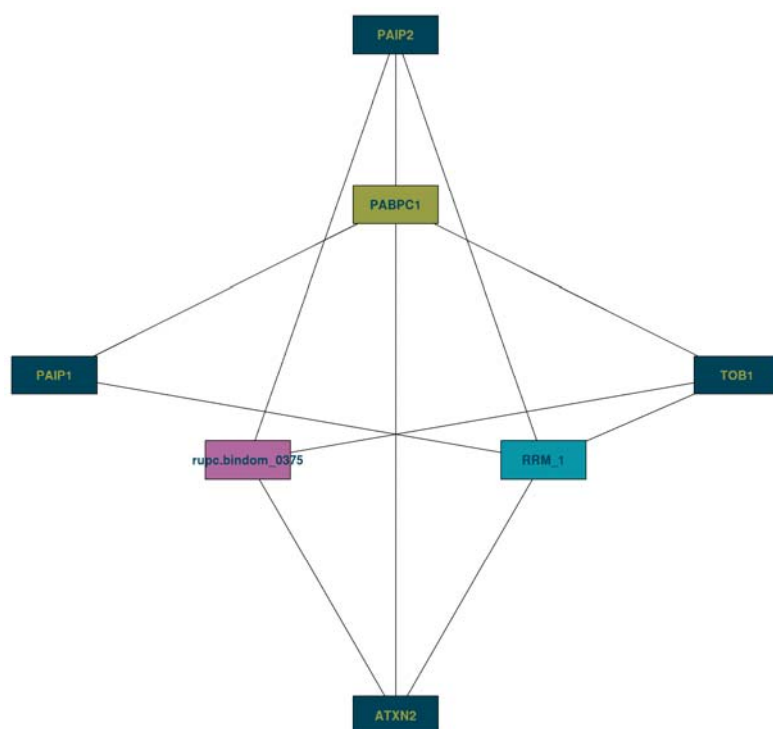


Supplementary Fig. S3. PPI compilation strategies applied to PDE6D interactome.

Full compiled interactome for Retinal rod rhodopsin-sensitive cGMP 3',5'-cyclic phosphodiesterase subunit delta (PDE6D) with evidence types. Black double-line, "complex-enriched" interaction; green dashed line, yeast-two hybrid; single black line, other interaction evidence. Spokes returning the CAAX box motif are highlighted in green. For each compilation strategy, rejected interactors are faded.

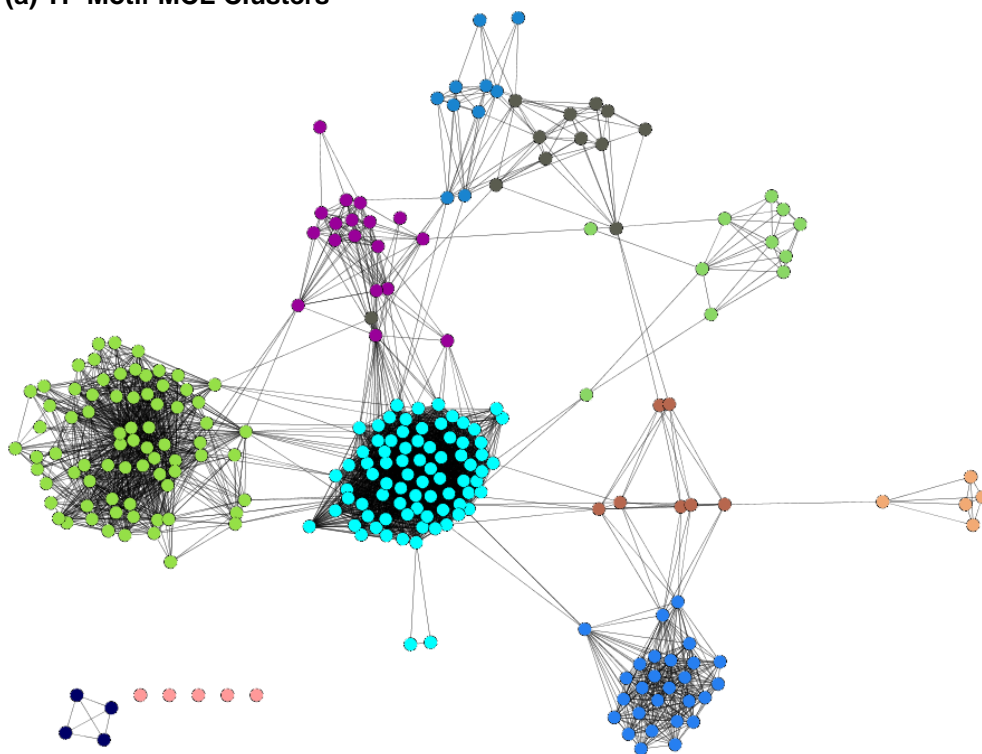


Supplementary Fig. S4. Ubiquitin Interacting Motif (UIM) sequence profile. The LQxxL motif matches positions 7-11 of the UIM. Sequence Logo from <http://pfam.sanger.ac.uk/>.

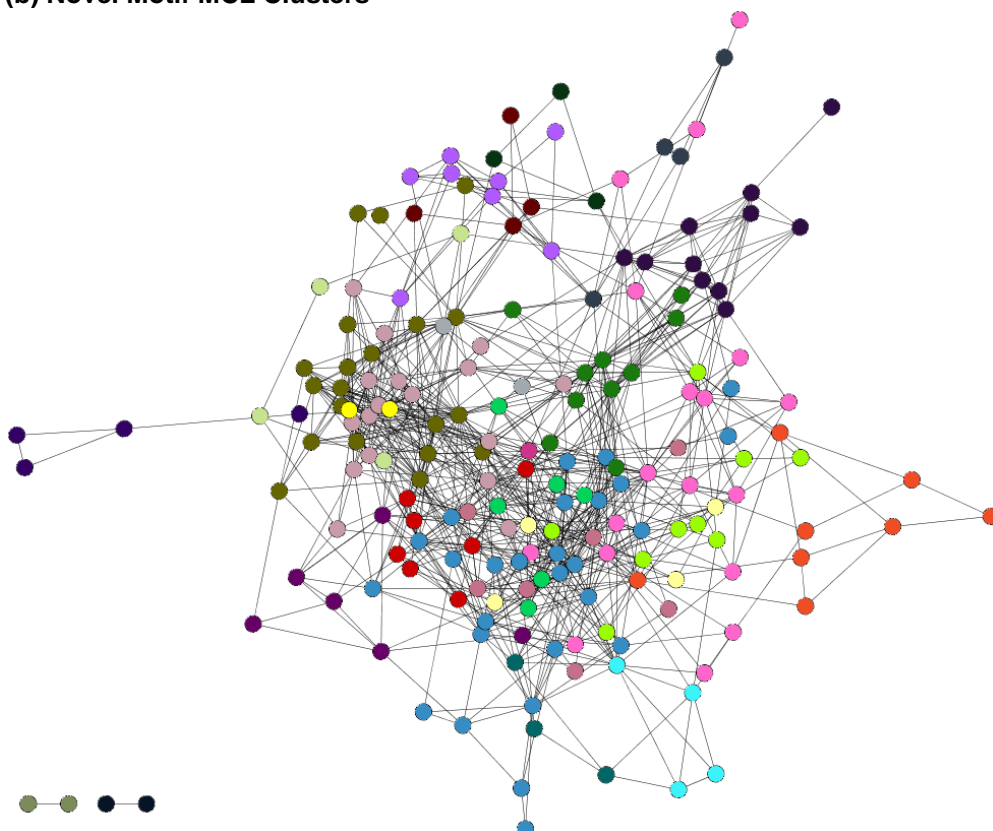


Supplementary Fig. S5. Hubs and spokes returning the SxLxxNaxxF motif, part of the PABPC1 interacting region. Hubs returning the motif are in the inside with spokes containing the motif around the outside. Lines joining hubs and spokes indicate spoke membership in the hub datasets. In addition to the True Positive hub PABPC1, spokes containing SxLxxNaxxF are also found in one Off-Target domain (RRM_1) and one random UPC dataset. Variants of this motif are also returned by the PABP domain (not shown).

(a) TP Motif MCL Clusters



(b) Novel Motif MCL Clusters



Supplementary Fig. S6. MCL clustering of (a) TP and (b) Novel SLiMs based on ComapriMotif similarity.

Each node is a motif, with each edge representing a ComapriMotif similarity match. Each colour represents a different MCL cluster. Details of clusters can be found in Supplementary Table S3.

Supplementary Tables

Supplementary Table S1. Significant True Positive SLiM Predictions

Known SLiM			Significant True Positive SLiMfinder predictions				
Name	Description		Hubs	ppi	y2h	bin	com
LIG_1433	Dominant 14-3-3 ligand motif (Variation of ELM:LIG_14-3-3_1). Expanded RS.S.P motif - [HKR][ST].[ST].P.	Genes	SFN	[ILV].[KR][ST].[ST] (3.77e-07)		[IL].[KR][ST].S (3.22e-05)	[ILV].[KR][ST].[ST] (2.89e-07)
			YWHAB	[LM].[HR][ST].S (7.41e-06)	RS.S.P (0.024)		[LM].[HR][ST].S (7.69e-07)
			YWHAG	R[ST]R[ST].S (1.44e-06)			RSR[ST].S (0.005)
			YWHAH	[LM].[HKR][ST].[ST] (2.64e-07)		R[ST].S[IMV] (8.65e-04)	R[ST].S[FLMV] (1.09e-07)
			YWHAQ	[FHY][HR].R..S (6.28e-06)			[FHY][HR].R..S (7.42e-06)
		Domain	14-3-3	FR.R..S (3.41e-04)	RS.S.P (0.009)		RS.S (2.35e-04)
				RS.S (5.23e-08)	RS.S.P (2.59e-05)	[ILM].[HKR][ST].S (9.02e-04)	RS.S (1.25e-06)
LIG_AP_GAE	Simplified Gamma-adaptin ear ligand motif, [DE][DE][DE]F.[DE]F (ELM LIG_AP_GAE_1)	Genes	AP1G1	FADF.S (0.041)			
			GGA2	FADF.S (0.007)			
		Domain	GAT	FADF.S (0.015)			
LIG_BRCT	SxxF Phosphomotif interacting with BRCA1	Gene	MAPK10	T.S..F.F (0.015)			
LIG_CtBP	PxDLS CtBP interaction ligand (ELM LIG_CtBP)	Genes	CTBP1	P[ILM]DL (2.52e-05)	P[IL]DL (7.05e-04)	P[IL]DL (0.004)	P[IL]DL (2.55e-05)
			CTBP2		D..[IL]DL (0.007)	D..[IL]DL (0.007)	
LIG_CYC	Cyclin recognition motif, [RK].L (ELM LIG_CYCLIN_1, MnM PBMCY00002A)	Domain	Cyclin_N	EE..R.L (2.57e-04)			EE..R.L (0.012)
LIG_Dyn	KxTQT Dynein Light Chain ligand (ELM LIG_Dynein_DLC8_1)	Gene	DYNLL2	K.TQ (0.049)			

LIG_EH	Canonical Eps15 homology (EH) domain binding motif, NPF (ELM LIG_EH_1)	Genes	EPS15 EPS15L1	NP[FY] (0.007) S..NP[FV] (7.67e-04)	n/a	n/a	S..NP[FV] (0.002)
LIG_GoLoco	Part of G-protein G-alpha domain binding motif (MnM PBMGPC00002A)	Domain	G-alpha		Q..R.D.QR (0.009)	Q..R.D.QR (0.017)	
LIG_PABPC1	PABPC1 binding region	Gene Domain	PABPC1 PABP	S.L..NA..F (3.38e-07) L..NA..F.P (3.89e-05)		L..NA..F.P (3.51e-10) L..NA..F.P (1.19e-07)	S.L..NA..F (1.64e-07) L..NA..F.P (1.84e-05)
LIG_PCNA	Q..[IL]..FF PCNA ligand (ELM LIG_PCNA)	Gene	PCNA	Q..[IL]..FF (4.28e-08)			Q..[IL]..FF (1.54e-08)
LIG_PDZ	Canonical C-terminal PDZ motif [ST].[ILV]\$. (ELM LIG_PDZ_1) See also generic PTS1 targetting motif TRG_PTS1	Genes	CASK DLG1 DLG2 DLG3 DLG4 DLGAP1 ERBB2IP GIPC1 GOPC INADL MAG11 MAG12 MAG13 PDZD3 PDZK1 RGS3 SLC9A3R1 SLC9A3R2 SNTA1 SNTB1	[ST].V\$ (2.48e-05) E[ST]..\$ (0.00e+00) E[ST]..\$ (0.00e+00) [ST].[LV]\$ (0.00e+00) [ST].[LV]\$ (0.00e+00) [ST].[LV]\$ (0.004) [ST].V\$ (0.020) S.V\$ (0.007) S.V\$ (7.12e-05) [ST].[LV]\$ (3.46e-11) [ST].[LV]\$ (1.16e-05) [ST].[LV]\$ (3.03e-05) [ST].V\$ (3.85e-09) T.[FL]\$ (9.06e-06) [ST].[FLM]\$ (1.02e-12) E[ST]..\$ (0.014) T.L\$ (0.00e+00) T.[LM]\$ (0.00e+00) E[ST]..\$ (9.57e-13) E[ST]..\$ (4.94e-08)	[ST].V\$ (4.30e-13) [ST].V\$ (2.87e-08) [ST].[LV]\$ (8.82e-11) [ST].[LV]\$ (1.22e-15) T.[LV]\$ (5.03e-06)	[ST].V\$ (5.28e-13) [ST].V\$ (2.87e-08) [ST].[LV]\$ (2.33e-09) E[ST].V\$ (1.11e-16) S.V\$ (0.006) S.V\$ (5.23e-05) [ST].V\$ (2.78e-12) [ST].[LV]\$ (4.15e-06) [ST].V\$ (3.85e-09) T.[FL]\$ (9.06e-06) [ST].[FL]\$ (3.16e-10) E[ST]..\$ (0.002) T.[LM]\$ (9.33e-15) T.[LM]\$ (4.77e-15) E[ST]..\$ (1.04e-07)	E[ST].V\$ (1.40e-08) E[ST]..\$ (6.46e-06) [ST].V\$ (4.00e-15) [ST].V\$ (0.011) n/a T.[FM]\$ (2.81e-05) [ST].[LM]\$ (5.77e-15) T.[LM]\$ (5.31e-10) E[ST]..\$ (0.029)

			SNTB2	E..[IV]\$ (1.67e-05)			
			SNTG1	ET..\$ (0.037)	n/a		ET..\$ (0.023)
			TJP1	T[HR][LV]\$ (1.67e-04)			D..V\$ (0.008)
			USH1C	T.L\$ (0.007)	T.L\$ (0.002)		T.L\$ (0.003)
		Domains	EBP50_C-term	T.L\$ (0.00e+00)	T.[LM]\$ (2.91e-14)		T.[LM]\$ (0.00e+00) [ST],[LM]\$ (0.00e+00)
			PDZ	n/a	[ST].[FLMV]\$ (3.25e-13)		[ST].[FILMV]\$ (2.18e-14) [ST].[FILMV]\$ (2.40e-08)
LIG_PP1	PP1 docking motif [RK].[0,1][IV][^P][FW] (ELM LIG_PP1)	Gene	PPP1CA	K[KR]V.F (4.03e-06)	K[KR]V.F (1.25e-07)		K[KR]V.F (5.28e-08)
LIG_PTB	NPxY Phopshotyrosine binding (PTB) motif (ELM LIG_PTB_1)	Gene	DAB2	P..F.NP.Y (5.48e-04)			P..F.NP.Y (1.11e-04)
LIG_SH2	SH2 domain ligand. Strongest YxN (GRB2) and YxxQ (STAT3) and YxxP (MnM) motifs only. Many other SH2 motifs might be part of the MOD_pY Generic motif.	Genes	GRAP2	DY.N[LM] (0.007)			DY.N[LM] (1.90e-04)
			GRB2	DY[MV]N (2.06e-04)			DY[MV]N (3.08e-04)
			LCK				E..P.Y.NL (0.039)
			LCP2	D[HY]EN (0.009)	n/a		n/a
			PTPN1		n/a		[DE]Y.N.S (0.010)
			SYK	YEN (8.11e-05)	n/a		YEN (0.020)
		Domain	SH2	n/a			[DE]Y[MV]N (0.014)
LIG_SH3	Canonical PxxP SH3 ligand motif.	Gene	FYN	P..P.[KR][KR] (0.005)			
LIG_WW_1	PPxY WW ligand motif (ELM LIG_WW_1)	Domains	WW	PP.Y (0.042)			PP.Y (0.027)
MOD_CAAXbox	Generic CAAX box prenylation motif Cx[ILMV]x\$ (ELM MOD_CAAXbox)	Gene	PDE6D	C.[IL].\$ (3.33e-06)			C.L.\$ (0.045)
		Domain	GMP_PDE_delta	C.[IL].\$ (0.001)			
MOD_CK1	Sxx[ST] Motif recognised by CK1 for Ser/Thr phosphorylation (ELM	Genes	CAMK2G	S..[ST]..[WY]G (0.007)	n/a		
			RPS6KA1		n/a		S.HS.Y (0.010)
			SRC	S..T..TP (0.002)			

	MOD_CK1_1)	Domain	Pkinase_C				D..[ST]I.S (0.013)
MOD_CK2	CK2 phosphorylation motif. Core ELM [ST]..E motif expanded to [ST]..[DE] (MiniMotif Miner).	Genes	CSNK2A1	SD.E (0.034)			
		Domain	MAPKAPK2	R..S.[IV]E (0.001)			
			PI3_PI4_kinase	SD.E (0.015)			SD.E (1.34e-04)
MOD_GSK3	[ST]xxx[ST] Site recognised by GSK3 for Ser/Thr Phosphorylation (ELM MOD_GSK3_1)	Genes	GSK3B				TP..[ST]P (0.032)
			PIK3R1				DSG..S (0.002)
MOD_PKB	R.R..[ST][^P] PKB Phosphorylation site (ELM MOD_PKB_1)	Genes	AKT1	R.R..S (2.19e-06)			R.R[ST].S (0.004)
			SGK1	R.R[ST].S (0.029)			
		Domain	Pkinase_C	R.R..S (2.35e-05)			
MOD_PKC	PKC phosphorylation motif, [ST].[KR] [MnM]	Gene	PRKAB1			A.GT.R (0.018)	
		Domain	AMPKBI			A.GT.R (0.018)	
MOD_STP	Common recurring phosphorylation motif [ST]P	Genes	CDK2	TPT (0.049)			
			GSK3B	P.SP (0.002)		P.SP (0.029)	TP..[ST]P (0.032)
			MAPK14	P.SP (0.004)			
			MAPK9	T.SP.F.F (0.033)			
			NEK2		TPY (0.007)	TPY (0.036)	
			SRC	S..T..TP (0.002)			
			YWHAH	SP..SP (6.21e-05)			P.SP..[FY] (0.009)
			YWHAQ	SP..SP (0.009)			
		Domains	14-3-3	P..[ST]P (7.12e-04)			P..[ST]P (0.009)
			Pkinase	n/a	P..[ST]P (0.002)	n/a	n/a
			Pkinase_C	P.[ST]P (5.09e-04)		P.SP..[FWY] (0.001)	
MOD_SUMO	Canonical sumoylation motif, [AILMV]K.E (ELM MOD_SUMO)	Gene	SUMO1	[ILV]K.E..[DE] (0.013)			
Yxx#	Multifunctional Yxx[ILMV] motif, which includes ITAM, ITIM, ITSM, SH2 and endocytic	Genes	CSK	Y..V.K (0.025)			
			GRAP2	DY.N[LM] (0.007)			DY.N[LM] (1.90e-04)
			GRB2	DY[MV]N[MV] (0.010)	Y.EV[FH] (0.016)	Y.EV[FH] (0.001)	DY[MV]N[MV] (7.64e-04)

targetting motifs.	LCK				E..P.Y.NL (0.039)
	PRKG1	N..Y..[FY] (0.035)			
	PTK2B	E..Y..M..F (0.040)			
	PTPN11	YA.[ILMV] (3.21e-05)			[ILV].YA.L (1.26e-04)
	PTPN6	YA.[ILV] (7.39e-04)	[IL].YA.L (0.004)	[IL].YA.L (0.032)	
	RIPK1				Y..L.H..Q (0.029)
	ZAP70	Y[DE].[LV] (0.009)	n/a		
	Domains	DSPc	NY..[MV]..H (0.007)		
		ITAM			P.Y.N[FL] (0.042)
		SH2	n/a		DY[MV]N[MV] (0.020)

Supplementary Table S2. PCNA interactors returning SLiM predictions.

Gene	Evidence	ppi ^a	bin ^a	com ^a	y2h ^a
ANXA2	BioGrid:affinity capture-ms; BioGrid:affinity capture-western	None	-	None	-
APEX1	BioGrid:reconstituted complex; HPRD:in vivo	None	-	D[FIL].N	-
APEX2	BioGrid:affinity capture-western; BioGrid:reconstituted complex; HPRD:in vitro; HPRD:in vivo	None	None	[ILV]..[FWY]F [ILV]..[FHY]F	-
BARD1	IntAct:pull down	None	-	None	-
BAZ1B	HPRD:in vitro	None	-	-	-
CCNA2	BioGrid:affinity capture-western; DIP:coimmunoprecipitation	None	-	None	-
CCNB1	HPRD:complex; HPRD:in vivo	None	-	D[FIL].N	-
CCND1	BioGrid:affinity capture-western; BioGrid:reconstituted complex; HPRD:complex; HPRD:in vitro	None	-	None	-
CCND3	BioGrid:reconstituted complex; HPRD:in vitro	None	-	None	-
CCNO	BioGrid:affinity capture-ms; BioGrid:reconstituted complex; DIP:coimmunoprecipitation; DIP:fluorescence microscopy; DIP:two hybrid; HPRD:in vitro; HPRD:yeast 2-hybrid	None	None	None	None
CDAN1	DIP:affinity chromatography technology; DIP:biochemical; DIP:fluorescence microscopy; DIP:x-ray crystallography	None	-	-	-
CDC2	HPRD:complex; HPRD:in vitro	None	-	None	-
CDC25C	BioGrid:affinity capture-western; BioGrid:reconstituted complex; BioGrid:two-hybrid; HPRD:in vitro; HPRD:in vivo; HPRD:yeast 2-hybrid	None	None	D[FIL].N	None
CDC6	BioGrid:two-hybrid; HPRD:yeast 2-hybrid	None	None	-	None
CDK2	BioGrid:affinity capture-western; DIP:affinity chromatography technology; DIP:biophysical; DIP:coimmunoprecipitation; HPRD:complex; HPRD:in vitro	None	-	None	-
CDK4	BioGrid:affinity capture-western; HPRD:complex	None	-	None	-
CDK5	HPRD:complex; HPRD:in vitro	None	-	None	-
CDK6	HPRD:in vivo	None	-	-	-
CDKN1A	BioGrid:affinity capture-western; BioGrid:co-crystal structure; BioGrid:reconstituted complex; BioGrid:two-hybrid; DIP:coimmunoprecipitation; DIP:cosedimentation through density gradient; HPRD:complex;	None	None	None	None

	HPRD:in vitro; IntAct:far western blotting; IntAct:two hybrid pooling; MINT:anti bait coimmunoprecipitation; MINT:two hybrid					
CDKN1C	BioGrid:affinity capture-western; BioGrid:reconstituted complex; BioGrid:two-hybrid; HPRD:in vitro; HPRD:in vivo	None	None	I..FF [ILV]..[FWY]F [ILV]..[FHY]F	None	
CDKN2A	IntAct:anti bait coip; IntAct:fluorescence imaging; IntAct:pull down	None	-	None	-	
CDT1	HPRD:in vitro; HPRD:in vivo; MINT:anti bait coimmunoprecipitation; MINT:gst pull down	None	-	[ILV]..[FWY]F [ILV]..[FHY]F	-	
CHAF1A	BioGrid:reconstituted complex; HPRD:in vitro; HPRD:in vivo; HPRD:yeast 2-hybrid; IntAct:anti bait coip; MINT:gst pull down	None	None	None	None	
CHTF18	BioGrid:affinity capture-ms; BioGrid:affinity capture-western; HPRD:in vitro; HPRD:in vivo	None	-	None	-	
CLSPN	BioGrid:affinity capture-western	None	-	I..FF [ILV]..[FWY]F [ILV]..[FHY]F	-	
CSTF1	IntAct:pull down	None	-	None	-	
DHX9	HPRD:complex; HPRD:in vitro	None	-	D[FIL].N	-	
DNA2	Reactome:reaction	None	-	-	-	
DNMT1	BioGrid:affinity capture-western; BioGrid:reconstituted complex; HPRD:in vitro	None	-	D[FIL].N D[FIL].N [ILV]..[FHY]F	-	
DNTT	BioGrid:co-purification; BioGrid:reconstituted complex; BioGrid:two-hybrid; HPRD:in vitro; HPRD:in vivo; HPRD:yeast 2-hybrid	None	None	None	None	
DNTTIP2	HPRD:in vitro	None	-	-	-	
EIF1B	IntAct:anti bait coip	None	-	None	-	
EP300	BioGrid:affinity capture-western; BioGrid:reconstituted complex; HPRD:in vitro; HPRD:in vivo	None	-	D[FIL].N	-	
EPB41	IntAct:anti bait coip	None	-	None	-	
ERCC5	BioGrid:reconstituted complex; DIP:affinity chromatography technology; DIP:biochemical; HPRD:in vitro; HPRD:in vivo	None	-	I..FF [ILV]..[FWY]F [ILV]..[FHY]F	-	
FEN1	BioGrid:affinity capture-western; BioGrid:co-purification; BioGrid:reconstituted complex; BioGrid:two-hybrid; DIP:affinity chromatography technology; DIP:biochemical; DIP:two hybrid; HPRD:in vitro;	Q..[IL]..FF	None	Q..[IL]..FF [ILV]..[FWY]F [ILV]..[FHY]F Q..L..FF	None	

	HPRD:in vivo; HPRD:yeast 2-hybrid; IntAct:fret; IntAct:two hybrid array; IntAct:two hybrid pooling; Reactome:direct_complex; Reactome:reaction				
FTSJ1	IntAct:anti bait coip	None	-	None	-
GADD45A	BioGrid:affinity capture-western; BioGrid:far western; BioGrid:reconstituted complex; BioGrid:two-hybrid; DIP:coimmunoprecipitation; DIP:two hybrid; HPRD:in vitro; HPRD:in vivo; HPRD:yeast 2-hybrid	None	None	None	None
GADD45B	BioGrid:affinity capture-western; BioGrid:reconstituted complex; BioGrid:two-hybrid; HPRD:in vitro; HPRD:in vivo; HPRD:yeast 2-hybrid	None	None	None	None
GADD45G	BioGrid:affinity capture-western; BioGrid:reconstituted complex; BioGrid:two-hybrid; DIP:affinity chromatography technology; DIP:coimmunoprecipitation; DIP:two hybrid; HPRD:in vitro; HPRD:in vivo; HPRD:yeast 2-hybrid	None	None	None	None
HDAC1	BioGrid:affinity capture-western; BioGrid:reconstituted complex; HPRD:in vitro; HPRD:in vivo	None	-	None	-
HLA-B	IntAct:anti bait coip	None	-	None	-
HLA-C	IntAct:anti bait coip	None	-	None	-
HLTF	DIP:anti tag coimmunoprecipitation; DIP:pull down	None	-	None	-
HPRD13123	HPRD:in vivo	-	-	-	-
HPRD16797	HPRD:in vivo	-	-	-	-
HUS1	BioGrid:affinity capture-western; BioGrid:two-hybrid; HPRD:yeast 2-hybrid	None	None	None	None
IKBKE	IntAct:anti bait coip	None	-	None	-
ING1	BioGrid:affinity capture-western; BioGrid:co-fractionation; DIP:biochemical; DIP:coimmunoprecipitation; HPRD:in vitro; HPRD:in vivo	None	-	None	-
KCTD13	BioGrid:far western; BioGrid:reconstituted complex; HPRD:in vitro; HPRD:in vivo	None	-	None	-
KIAA0101	BioGrid:affinity capture-western; BioGrid:two-hybrid	Q..[IL]..FF	None	Q..[IL]..FF I..FF [ILV]..[FWY]F [ILV]..[FHY]F	None
LIG1	BioGrid:affinity capture-ms; HPRD:in vitro	Q..[IL]..FF Q.[ST][IL]..FF	-	Q..[IL]..FF Q.[ST][IL]..FF I..FF [ILV]..[FWY]F	-

MCC	IntAct:anti bait coip	None	-	[ILV]..[FHY]F D[FIL].N	-
MCL1	BioGrid:affinity capture-western; BioGrid:reconstituted complex; BioGrid:two-hybrid; HPRD:in vitro; HPRD:in vivo; HPRD:yeast 2-hybrid	None	None	D[FIL].N	None
MME	IntAct:anti bait coip	None	-	None	-
MSH2	BioGrid:affinity capture-ms; HPRD:in vitro	None	-	None	-
MSH3	BioGrid:affinity capture-ms; BioGrid:affinity capture-western; BioGrid:far western; BioGrid:protein-peptide; HPRD:in vitro; HPRD:in vivo	Q..[IL]..FF	-	Q..[IL]..FF [ILV]..[FWY]F [ILV]..[FHY]F Q..L..FF	-
MSH6	BioGrid:affinity capture-ms; BioGrid:affinity capture-western; BioGrid:far western; BioGrid:protein-peptide; HPRD:in vitro; HPRD:in vivo	Q..[IL]..FF Q.[ST][IL]..FF TL.SFF	-	Q..[IL]..FF Q.[ST][IL]..FF [ILV]..[FWY]F [ILV]..[FHY]F TL.SFF Q..L..FF	-
MUTYH	BioGrid:affinity capture-western; BioGrid:reconstituted complex; HPRD:in vitro; HPRD:in vivo	Q..[IL]..FF	-	Q..[IL]..FF [ILV]..[FWY]F [ILV]..[FHY]F Q..L..FF	-
MYBBP1A	BioGrid:affinity capture-ms; HPRD:in vitro	None	-	None	-
OTUB1	BioGrid:affinity capture-ms	None	-	None	-
PARP1	BioGrid:affinity capture-western; HPRD:in vivo	None	-	D[FIL].N	-
PCNA	BioGrid:co-purification; DIP:x-ray crystallography; HPRD:complex; HPRD:in vitro	None	-	None	-
POLA1	HPRD:complex; Reactome:reaction	None	-	None	-
POLA2	Reactome:reaction	None	-	-	-
POLB	HPRD:in vivo; HPRD:yeast 2-hybrid	None	None	-	None
POLD1	BioGrid:affinity capture-ms; BioGrid:invitro; BioGrid:invivo; HPRD:complex; HPRD:in vitro; HPRD:in vivo; IntAct:anti bait coip; IntAct:far western blotting; Reactome:reaction	None	-	None	-
POLD2	BioGrid:far western; BioGrid:reconstituted complex; HPRD:in vitro; HPRD:in vivo; IntAct:anti bait coip; Reactome:reaction	None	-	None	-
POLD3	BioGrid:affinity capture-ms; BioGrid:reconstituted complex; HPRD:in vitro; IntAct:anti tag coip; IntAct:confocal microscopy; IntAct:far western blotting; IntAct:fret; MINT:two hybrid; Reactome:reaction	Q..[IL]..FF Q.[ST][IL]..FF	None	Q..[IL]..FF Q.[ST][IL]..FF I..FF [ILV]..[FWY]F [ILV]..[FHY]F	None

POLD4	HPRD:in vitro; HPRD:yeast 2-hybrid; IntAct:elisa; IntAct:far western blotting; Reactome:reaction	None	None	-	None
POLDIP2	BioGrid:affinity capture-western; BioGrid:reconstituted complex; BioGrid:two-hybrid; HPRD:in vitro; HPRD:in vivo; HPRD:yeast 2-hybrid	None	None	None	None
POLE	BioGrid:affinity capture-ms; HPRD:in vitro; Reactome:reaction	None	-	D[FIL].N	-
POLE2	Reactome:reaction	None	-	-	-
POLH	BioGrid:reconstituted complex; BioGrid:two-hybrid; HPRD:in vitro; HPRD:yeast 2-hybrid; MINT:gst pull down; MINT:two hybrid	TL.SFF	None	[ILV]..[FWY]F [ILV]..[FHY]F TL.SFF	None
POLI	MINT:gst pull down; MINT:two hybrid	None	None	[ILV]..[FWY]F [ILV]..[FHY]	None
POLL	BioGrid:reconstituted complex; HPRD:in vitro; HPRD:in vivo	None	-	None	-
POLM	HPRD:in vitro	None	None	-	-
PPP1CC	IntAct:antibody array	None	-	-	-
PRIM1	Reactome:reaction	None	-	-	-
PRIM2	HPRD:complex; Reactome:reaction	None	-	None	-
PRKDC	BioGrid:affinity capture-ms; HPRD:in vitro	None	-	None	-
PTMA	HPRD:in vitro	None	-	-	-
PTP4A3	IntAct:anti bait coip	None	-	None	-
RAD17	DIP:fluorescence microscopy	None	-	-	-
RAD18	HPRD:complex	None	-	None	-
RAD9A	DIP:coimmunoprecipitation; HPRD:in vitro	None	-	D[FIL].N	-
RELA	IntAct:tap; MINT:anti tag coimmunoprecipitation	None	-	None	-
RFC1	BioGrid:affinity capture-ms; BioGrid:affinity capture-western; BioGrid:reconstituted complex; HPRD:complex; HPRD:in vitro; HPRD:in vivo; Reactome:reaction	None	-	I.FF [ILV]..[FWY]F [ILV]..[FHY]F	-
RFC2	BioGrid:affinity capture-ms; BioGrid:reconstituted complex; HPRD:complex; HPRD:in vitro; Reactome:reaction	None	-	None	-
RFC3	BioGrid:affinity capture-ms; BioGrid:affinity capture-western; HPRD:complex; HPRD:in vitro; HPRD:in vivo; Reactome:reaction	None	-	None	-
RFC4	BioGrid:affinity capture-ms; BioGrid:affinity capture-western; BioGrid:reconstituted complex; DIP:coimmunoprecipitation; HPRD:complex; HPRD:in vitro;	None	-	None	-

RFC5	HPRD:in vivo; Reactome:reaction BioGrid:affinity capture-ms; BioGrid:reconstituted complex; HPRD:complex; HPRD:in vitro;	None	-	None	-
RPA1	Reactome:reaction BioGrid:affinity capture-ms; HPRD:complex; HPRD:in vitro; Reactome:reaction	None	-	D[FIL].N [ILV]..[FWY]F	-
RPA2	Reactome:reaction	None	-	-	-
RPA3	Reactome:reaction	None	-	-	-
RUVBL2	BioGrid:affinity capture-ms	None	-	None	-
SEC23IP	HPRD:in vitro	None	-	-	-
SMARCA4	BioGrid:co-fractionation	None	-	-	-
SUB1	HPRD:yeast 2-hybrid	None	None	-	None
TCOF1	HPRD:in vitro	None	-	-	-
TIMELESS	BioGrid:affinity capture-western	None	-	None	-
TOP1	HPRD:complex	None	-	None	-
TRAF6	IntAct:anti bait coip	None	-	None	-
TSC22D1	IntAct:anti bait coip	None	-	None	-
UBA52	DIP:anti bait coimmunoprecipitation; DIP:anti tag coimmunoprecipitation; DIP:comigration in sds page; MINT:his pull down	None	-	None	-
UBB	DIP:anti bait coimmunoprecipitation; DIP:anti tag coimmunoprecipitation; DIP:comigration in sds page; HPRD:in vivo; MINT:his pull down	None	-	None	-
UBC	BioGrid:affinity capture-western; DIP:anti bait coimmunoprecipitation; DIP:anti tag coimmunoprecipitation; DIP:comigration in sds page; MINT:his pull down	None	-	None	-
UBE2B	HPRD:complex	None	-	None	-
UNG	BioGrid:affinity capture-ms; BioGrid:reconstituted complex; HPRD:in vitro	Q..[IL]..FF Q.[ST][IL]..FF TL.SFF	-	Q..[IL]..FF Q.[ST][IL]..FF [ILV]..[FWY]F [ILV]..[FHY]F TL.SFF Q..L..FF	-
WRN	BioGrid:affinity capture-western; BioGrid:reconstituted complex; HPRD:in vitro; HPRD:in vivo; MINT:fluorescence microscopy	None	-	[ILV]..[FWY]F [ILV]..[FHY]F	-
XRCC1	BioGrid:affinity capture-western; BioGrid:co-localization; BioGrid:fret; BioGrid:reconstituted complex; HPRD:in vitro; HPRD:in vivo; HPRD:yeast 2-hybrid	None	None	D[FIL].N	None
XRCC5	BioGrid:affinity capture-ms; BioGrid:affinity capture-western; HPRD:in vitro; HPRD:in vivo	None	-	None	-
XRCC6	BioGrid:affinity capture-ms; BioGrid:affinity capture-western; HPRD:in vitro; HPRD:in vivo	None	-	None	-
YBX1	BioGrid:affinity capture-western; BioGrid:reconstituted complex;	None	-	None	-

HPRD:in vitro;
 HPRD:in vivo

a. None, no significant motif returned in this spoke; -, spoke not in dataset.

Supplementary Table S3. MCL clusters of TP and novel motifs returned from Real datasets, connected by ⁵ CompariMotif similarity.

MCL ^a	Rank ^b	Nodes ^c	Edges ^c	Density ^c	Members ^d	Novel ^e	TP ^e
Real	1	82	2309	0.348	C.K.K, FR.R..S, FR.R[ST].S, K.[KR]..A..CR, K.[KR]..A..[KR], L.R..S, L.R.S.S[FM], L.R[ST].S[MV], L.[HR][ST].S, Q[KR].R, R..S.P, R..S.S, R..S.[IV]E, R..SAP, R.NS, R.R..S, R.R.R, R.RH.S, R.RS, R.RS.S, R.RT.S, R.R[ST].S, R.R[ST].[ST], RS.S, RS.S..[FH], RS.S.P, RS.S[LMV], RSR[ST].S, RT.S, R[ST].S..[DE], R[ST].S.P, R[ST].SAP, R[ST].S[FLMV], R[ST].S[IMV], R[ST].[ST][FLMV], R[ST]R[ST].S, R[ST]R[ST].[ST], R[ST][HR][ST].S, [FHY][HR].R..S, [FH]QRS.S, [FH]R.R..S, [FH][KR].R..[ST], [FLM].[HR][ST].S, [FL]R.R..S, [FY][HR].R..S, [HKR].RS.S, [HKR].RS.[ST], [HKR].R[ST].S, [HKR].R[ST].S[FLV], [HKR].[HKR][ST].[ST], [HKR][ST].S.[ST], [HKR][ST].[ST], [HKR][ST].[ST].P, [HR].R..S..[DE], [HR].R..[ST].P, [HR].R[ST].S, [HR].R[ST].[ST], [HR].R[ST][HKR].S, [HR].[HKR][ST].S, [HR].[HR][ST].S, [HR][ST].S, [HR][ST].[ST], [HR][ST]R[ST].S, [ILMV].[HKR][ST].[ST], [ILM].[HKR][ST].S, [ILV].[KR][ST].[ST], [IL].[KR][ST].S, [IL].[KR][ST].S.P, [IL][HR][KR][ST].S, [KR]N[HK], [KR]N[KR], [KR].S.S..D, [KR][ST].S.P, [KR][ST].S[LMV], [KR][ST].[ST], [KR][ST][KR][ST], [LMV].[HR][ST].S, [LM].[HKR][ST].S, [LM].[HKR][ST].[ST], [LM].[HR]..S.P, [LM].[HR][ST].S, [ST].SAP	7	75
Real	2	74	1131	0.209	D..L\$, D..V\$, D..[LM]\$, DT..\$, DT.L\$, DT.[LM]\$, E..T..\$, E..T.L\$, E..V\$, E..[ILV]\$, E..[IV]\$, E..[LV]\$, E.T..\$, E.T.L\$, EDT..\$, ES..\$, ES.V\$, ET..\$, ET.V\$, E[ST]..\$, E[ST].V\$, E[ST].[LV]\$, K.T.L\$, L.T..\$, L.T.V\$, L.[ST]..\$, L.[ST].V\$, LE..V\$, R.[ST]..\$, R.[ST].V\$, S.IE..V\$, S.V\$, T.L\$, T.M\$, T.V\$, T.[FL]\$, T.[FM]\$, T.[LM]\$, T.[LV]\$, TRL\$, TT.V\$, T[HKR].\$, T[HKR][LV]\$, T[HR]..\$, T[HR][LV]\$, T[KR].\$, T[KR]L\$, T[ST].[LV]\$, V..T..\$, [DE]..[LM]\$, [DE]S..\$, [DE][ST]..\$, [DE][ST].[ILMV]\$, [DE][ST].[ILV]\$, [DE][ST].[LMV]\$, [DE][ST].[LV]\$, [ILV].[ST].V\$, [IL].[ST]..\$, [IL].[ST].V\$, [ILE]..V\$, [KR]..T.V\$, [KR].T..\$, [KR].[ST]..\$, [KR].[ST].[LV]\$, [KR]L\$, [LV].[ST].V\$, [ST].L\$, [ST].V\$, [ST].[FILMV]\$, [ST].[FLMV]\$, [ST].[FLM]\$, [ST].[FL]\$, [ST].[LM]\$, [ST].[LV]\$, [ILM].[DE]N, [ST].[IL]N.N	0	74
Real	3	37	400	0.300	A.EF.P, G..WA..H, G.A..[FH], HL..IA, KN..AA, L..NA..F, L..NA..F.P, L..NA.EF, L..NAK.F, LN..A..F, LN..A..F.P, LN.NA, LN.NA.F, M.LL..N, N..A..F.P, N..A.EF, N..A.EF.P, N..AA, N.NA..F, N.NA..F, NA..F, NA..F.P, NA.EF, NP.A..F, NP.A..F.P, N[FL].AL, S..NPNA, S.L..N..EF, S.L..NA, S.L..NA..F, S.L..NA.E, S.L.PNA, S.LN.NA, V..[IV]LN, [FLV]NP.A, [ILMV].[DE]N, [ST].[IL]N.N	10	27
Real	4	20	138	0.363	FADF.S, K.V.F, K[KR]V.F, L.F.D, N..V.[FH], RP.T[FV].[IL], RV.F, RV.[FW]A, V.[FIV]C, VTF, VTF..[DE], V[ST]F.[DE], [KR].V.F.[DE], [KR].V[ST]F, [KR].[ILV].F, [KR].[ILV].[FW], [KR]K.V.F, [KR]V[ST]F, [KR][KR]..F, [LV].[FW].[DE]	3	17
Real	5	39	251	0.169	A.Q.A, A.[ILM]A, A.[LV].D[FL], A.[LV].[FH], AA.[KR], AA[FILMV], AA[FILV], AA[ILV], AM..A, A[FILMV]..A, A[FIV]..C, A[ILMV]..A, A[IM]..A, A[LV]..[FHY], CKA, H..[FY].K, I.A.E, M[FY]..L, NY..[MV]..H, Q..A.L, R..[FLV]..A, Y.EV[FH], YA.[ILMV], YA.[ILV], YA[ST][LV], [DE].[FILMV]..A, [DE][HY]..F..A, [FILV]..A[LV], [FIV]E.A, [FLMV]..A..A, [FLMV].[HKR]A, [FLV]..ALQ, [ILV].YA.L, [ILV].YA.[IL], [IL].EA[LMV], [IL].YA.L, [IV].Y..L.[FH], [IV].Y..L.[HK], [LV]..A.K	29	10
Real	6	17	69	0.254	D..[IM].F.L, G..G.F.L..E, G..G.G.F.L, G..V.L.C, G.G.F.L..E, GFG[FL], GFHL, H.LV, KG..G..F, KG..G..F.L, KG..G.G..L, KG..G.G.F, W..G[FL], [DE]..[LM].[FH].L, [DE].M..GL.D, [MV].[FHY].L.[DE], [MV].[FH].L.[DE]	17	0
Real	7	16	61	0.254	D..N..[FL], D..N.[FI], DY.N[LMV], DY.N[LM], DY[MV]N, DY[MV]N[MV], D[HY]EN, EK.YE, EN[LMV], YEN, YEN[LV], YVNV, Y[DE].[LV], [DE]Y.N.S, [FIL].D..N, [KR]EK[LM]	6	10
Real	8	19	73	0.213	A.Q.L, A.Q.[LV], ALWD, A[FIV]..L, A[FIV]..[LV], E..V..L.K.L, K..E[LV].D, L.D[LM]..D, L.[DE]A, LA.Q, Q.[FILMV].[DE], Q.[FLV].[DE],	19	0

TP	4	18	108	0.353	S.L..NA..F, S.L..NA.E, S.L.PNA, S.LN.NA, [ST].[IL]N.N EE..R.L, FADF.S, K.V.F, K[KR]V.F, RP.T[FV].[IL], RV.F, RV.[FW]A, VTF, VTF..[DE], V[ST]F.[DE], [KR].V.F.[DE], [KR].V[ST]F, [KR].[ILV].F, [KR].[ILV].[FW], [KR]K.V.F, [KR]V[ST]F, [KR][KR].F, [LV].[FW].[DE]	0	18
TP	5	12	43	0.326	DY.N[LMV], DY.N[LM], DY[MV]N, DY[MV]N[MV], D[HY]EN, SD.E, YEN, YEN[LV], YVNV, Y[DE].[LV], [DE]Y.N.S, [FY].N..Y	0	12
TP	6	10	33	0.367	NY..[MV].H, Y.EV[FH], YA.[ILMV], YA.[ILV], YA[ST][LV], [ILV].YA.L, [ILV].YA.[IL], [IL].YA.L, [IV].Y..L.[FH], [IV].Y..L.[HK]	0	10
TP	7	7	21	0.500	F.NP.Y, NPF, NP[FV], NP[FY], P..F.NP.Y, S..NP[FV], TNPF	0	7
TP	8	11	32	0.291	P..P.[KR][KR], P..[ST]P, P.SP, P.SP..[FWY], P.SP..[FY], P.[ST]P, S..T..TP, SP..SP, SP..[ST]P, TPY, [ST]P..[ST]P..[ST]	0	11
TP	9	5	10	0.500	D..[IL]DL, PLDL, P[ILMV]DL, P[ILM]DL, P[IL]DL	0	5
TP	10	4	6	0.500	I..FF, Q..[IL]..FF, Q.[ST][IL]..FF, [ILV]..[FWY]F	0	4
Novel	1	20	100	0.263	A.Q.A, AM..A, A[FILMV]..A, A[ILMV]..A, A[IM]..A, CKA, F.[HK].H[IV], H..[FY].K, I..A.E, L.[DE]A, R..[FLV]..A, [DE].[FILMV]..A, [DE][HY].F..A, [FILV]..A[LV], [FIV]E.A, [FLMV]..A..A, [FLMV].[HKR]A, [FLV]..ALQ, [IL].EA[LMV], [LV]..A.K	20	0
Novel	2	11	37	0.336	G..G..F.L.E, G..G.GF.L, G..V.L.C, G.GF.L.E, GFG[FL], GFHL, KG..G..F, KG..G..F.L, KG..G.G.L, KG..G.GF, W..G[FL]	11	0
Novel	3	27	89	0.127	A.Q.L, A.Q.[LV], A[FIV]..L, A[FIV]..[LV], D.F.VK, D.G[FL].C, G[IM][FY], K..E[LV].D, L.D[LM]..D, LA.Q, LQ..L, M..Q..[IL], Q..F.C, Q..[FM], Q.[FILMV].[DE], Q.[FLV].[DE], Q.[FL]..NN, QQ.[FILMV], Q[FY][LV].D, Q[KR]..[DE], RQ..[FLV], V.D.G, [FIL].D..N, [IV].[DE].F, [KR]..[DE].Q..L, [MV]Q.L.D, [MV]Q.L.D.L	27	0
Novel	4	17	50	0.184	A.[ILM]A, A.[LV].D[FL], A.[LV].[FH], AA.[KR], AA[FILMV], AA[FILV], AA[ILV], ALWD, A[FIV]..C, A[LV]..[FHY], G.VL.A.M, HL..IA, L.F.D, N..AA, N[FL].AL, Q..A.L, [FLV]NP.A	17	0
Novel	5	8	18	0.321	C.K.K, K.[KR]..A..CR, K.[KR]..A..[KR], KN..AA, Q[KR].R, R.R.R, [KR]N[HK], [KR]N[KR]	8	0
Novel	6	10	23	0.256	D..[IM].F.L, E..L..W, H.L.V, M[FY]..L, N..V.[FH], V.[FIV]C, [DE]..[LM].[FH].L, [DE].M..GL.D, [MV].[FHY].L.[DE], [MV].[FH].L.[DE]	10	0
Novel	7	7	14	0.333	E.LA, EE.E.[FLV], EE.E.[FV], EN[LMV], R..VE.[LM], [FH]EE[LV], [IV]..EV[DE]	7	0
Novel	8	11	23	0.209	D..N..[FL], L..EN..L, L..EN..[IL], M.LL..N, M.LL[KR].N, N..L..[DE], [HK].N.W, [ILMV].[DE]N, [KR]..GW, [KR].N..[KR], [LM].N..[FLV]	11	0
Novel	9	6	10	0.333	D.I..[FIL], D.I..[FLV], D.I..[LV], I.E.L, [DE]VI, [FI]G.[FV]D	6	0
Novel	10	4	6	0.500	Q..G..VNG, Q.[ILV]N, VNG, [IV]NG	4	0
Novel	11	6	9	0.300	A..[ILMV].Q, A..[IM]..Q, LA..I, N..A..[IV]L, Q.A..M, [IV]..QG	6	0
Novel	12	4	5	0.417	EK[FI].R.[HK], K..RWT, P..K..[KR], P.K..R	4	0
Novel	13	9	13	0.181	D.QL, D[KR].L.I.G, K..I.D, Q[FILV]..LQ, Q[LM]R, R.IRD, R.Q.R..R, [DE]E.L.Q[IM], [HR].[IL]R	9	0
Novel	14	8	11	0.196	D[FIL].N, F.N.R, N.[KR]I, P..F.N, WF.N.R, [FM]..NI, [FY].FN.K, [FY].[WY]..N	8	0
Novel	15	7	9	0.214	INPD, LN..[FI], V..[IV]LN, [FM].[IM]N, [ILMV].N..D, [IL].NM, [IL]N..[FV]	7	0
Novel	16	3	3	0.500	DRL..V, DRL..V.G, LQ.V	3	0
Novel	17	3	3	0.500	H[HY]H.P, H[LV][HR].H, [FH]HH.P	3	0
Novel	18	7	9	0.214	E.DI.V, I..[KR][LM]..[DE], [DE].[DE]..[MV]..G, [DE][FIL]..Q[LV], [DE][ILMV]..[HKR][FILV], [DE][ILV]A..L, [DE][IL].A	7	0
Novel	19	4	4	0.333	LE..R..[IL], R.G..R, R.GF.[KR], [KR]..[FLM].R	4	0
Novel	20	4	4	0.333	HWK, HWKQ, P.HW, [HY][FWY]D	4	0
Novel	21	4	3	0.250	DMG, D[IM].F..F, E..E..DF..L, E..[DE].M.F..[FL]	4	0
Novel	22	4	3	0.250	E..V..L.K.L, L..K..Q.E, L.KM.Q, [DE]..HL..KE	4	0
Novel	23	2	1	0.500	VAR, [MV]VA	2	0
Novel	24	2	1	0.500	EK.YE, [KR]EK[LM]	2	0
Novel	25	2	1	0.500	G..WA..H, G.A..[FH]	2	0
Novel	26	2	1	0.500	ERG.K, P..T.V..E.G	2	0

- MCL clustering run: Real, TP and novel; TP, TP only; Novel, novel only.
- Rank of cluster based on Score = Node number x Density.
- Number of Nodes (N) and Edges (E) in cluster. Density (D) is calculated as $D = E / (N(N-1))$.
- Patterns of predicted SLiMs in cluster.
- Numbers of Novel and TP SLiMs found in each cluster.