

S1 (table) | Structures of cullin–RING-ligase subunits, complexes, substrates and regulators

Structure	Species	Description	PDB accession number	References
SKP1–SKP2	Human	SCF adaptor/receptor	1FQV, 1FS1, 1FS2	1
CUL1–RBX1	Human	SCF enzymatic core	1LDJ	2
CUL1–RBX1–SKP1–F-box (SKP2)	Human	SCF model structure	1LDK	2
APC2 (773–846)	Human	Distant cullin homologue	1LDD	2
Skp1–Cdc4–CPD peptide	Yeast	Substrate recognition by SCF ^{Cdc4}	1NEX	3
SKP1– β -TrCP– β -catenin peptide	Human	Substrate recognition by SCF ^{β-TRCP}	1P22	4
Elongin-BC–VHL	Human	CUL2 complex adaptor/receptor	1VCB	5
Elongin-C–VHL peptide	Yeast	Cul2 complex adaptor/receptor	1HV2	6,7
Hydroxylated HIF1 α -peptide–elongin-BC–VHL	Human	Substrate recognition by VHL	1LQB, 1LM8	8,9
PML BTB domain	Human	CUL3 adaptor?	1CS3	10
BCL6 BTB domain	Human	CUL3 adaptor?	1R2B, 1R28, 1R29	11
PLZF BTB domain	Human	CUL3 adaptor?	1BUO	12
CBL–UBCH7	Human	E2 docked on RING E3	1FBV	2
Ubiquitin	Human	Monomer, tetramer chain	1UBQ, 1UBI, 1TBE, 1F9J	13–18
RUB1	<i>A. thaliana</i>	Monomeric RUB1	1BT0	19
NEDD8	Human	Monomeric NEDD8	1NDD	20
APPBP1–UBA3–NEDD8–ATP	Human	NEDD8-activating enzyme	1R4N, 1R4M	21,22
AfJAMM	<i>A. fulgidis</i>	Archaeobacterial homologue of Csn5	1R5X, 1O10	23,24

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S2 (table) | **Receptors and substrates of cullin–RING ligases that have been implicated in diverse biological processes**

Organism	Cullin	Receptor	Implicated substrate	Biological Process	References
<i>S. cerevisiae</i>	Cul1	Cdc4	Cdc6	DNA replication	1–3
			Ctf13	Cell cycle	4
			Far1	Cell cycle	5–7
			Gcn4	Transcription	8–10
			Sic1	Cell cycle	11–14
		Grr1	Cln1/2	Cell cycle	13,17,18
			Gic2	Cell polarity	6,19,20
		Met30	Grr1	Autoregulation	15,16
Met4	Transcription		21–25		
Mdm30	Met30	Autoregulation	24,26		
	Swe1	Cell cycle	27,28		
Ufo1	Fzo1	Mitochondrial shape	29		
?	?	Ho	Signal transduction	30,31	
		Cln3	Cell cycle	11,32	
		Ste7	Signal transduction	33	
<i>S. pombe</i>	Cul1	Pop1/Pop2	Cdc18	DNA replication	34–36
			Rum1	Cell cycle	34–36
			Cig2	Cell cycle	37
		?	Mid2p	Cell cycle	38
	Cul3	Btb3	Btb3	Autoregulation	39
Cul4	?	Spd1	DNA replication	40	
<i>C. elegans</i>	Cul1	SEL-10	LIN-12	Signal transduction	41
	Cul2	VHL	HIF-1	Transcription	42
		ZIF-1	PIE-1, POS-1, MEX-1/-5/-6	Development	43
	?	CKI-1	Cell cycle	44	
	Cul3	MEL-26	MEI-1	Cell cycle	45–49
Cul4	?	CDT-1	DNA replication	50	
<i>D. melanogaster</i>	Cul1	Archipelago	Cyclin E dMyc	Cell cycle Transcription	51 52
		Morgue	Diap1	Apoptosis	53
		Partner of Paired	Paired	Transcription	54,55
		Slimb	Armadillo Cactus Cubitus interruptus	Development Transcription Transcription	56–59 60,61 56,57,59,62

			Dorsal E2F	Transcription DNA replication	60 63
			Period	Circadian- clock regulation	64,65
			Relish Timeless	Transcription Circadian- clock regulation	66 65
	Cul4	?	Cdt1	DNA replication	67
<i>X. laevis</i>	Cul1	β-TrCP	β-catenin Xom	Development Development	68–71 72
		Tome-1	Wee1	Cell cycle	73,74
		?	Xic1	Cell cycle	75–77
<i>A. thaliana</i>	Cul1	COI1	RPD3b Rubisco (small subunit)	Transcription Photorespiration	78 78
		EBF1/EBF2 SLF-S2	EIN3 S-RNases	Transcription Signal transduction	79–81 82
		SLY1	RGA	Signal transduction	83,84
		SKP2 TLP9	E2Fc ?	Transcription Signal transduction	85 86
		TIR1	AUX/IAA proteins	Transcription	87–89
		UFO ZTL	AGAMOUS TOC1	Development Circadian- clock regulation	90 91
		Cul3	ETO1	ACS5	Signal transduction
	<i>H. sapiens/ M. musculus</i>	Cul1	β-TrCP1 and 2 (FBW1, HOS) + HIV: Vpu	ATF4	Transcription
β-catenin				Signal transduction	58,95–98
CDC25a CD4				Cell cycle Viral modulation	99,100 101
EMI1 IκBα				Cell cycle Transcription	102,103 60,95,98, 104–111
NFκB1/p105, NFκB2/p100 Prolactin receptor SMAD3/4				Transcription Signal transduction Signal transduction	112–118 119 120,121

		Type-I interferon receptor (IFNAR1)	Signal transduction	122
		WEE1	Cell cycle	123
	CDC4 (FBW7, SEL10)	Cyclin E	Cell cycle	124,125
		Jun	Transcription	126
		Myc	Transcription	127,128
		Notch1/4	Signal transduction	129,130
		Presenilin-1	Regulation	131
	FBS1 (FBX2, NFB42)	Glycoproteins	Protein quality control	132
		Herpes simplex virus type 1: UL9	Viral modulation	133
	FBS2	N-glycans	Protein quality control	134
	FBX4	α B-crystallin	Heat-shock protein	135
	SKP2 + Cyclin T1	B-MYB	Transcription	136
		CDK9	Transcription	137,138
		CDT1	Cell cycle	50,67, 139–141
		Cyclin D	Cell cycle	142–144
		Cyclin E	Cell cycle	145,146
		Papilloma virus: E7	Viral modulation	147
		E2A	Development	148
		E2F1	Transcription	149
		Myc	Transcription	150
		ORC1	DNA replication	151
		p57	Cell cycle	152
	+CKS1	p130	Cell cycle	153,154
	+CKS1	p21	Cell cycle	142,144,155, 156
	+CKS1	p27	Cell cycle	142,145, 157–160
Cul2	SOCS1/3	IRS1/2	Signal transduction	161
	SOCS1	TEL-JAK2	Cell cycle	162,163
		VAV	Signal transduction	164
	VHL	HIF1 α , HIF2 α	Transcription	165–175
		RPB7	Transcription	176
		RPB1	Transcription	177
		VDU1/2	Protein quality control	178,179
		hnRNP A2	Transcription	180
		PKC λ	Signal transduction	181

		STRA13	Transcription	182
Cul3	RhoBTB2	RhoBTB2	Cell cycle	183
	?	TOP1	DNA replication	184
	KEAP1	NRF2	Transcription	185,186
Cul4	DET1/COP1	Jun	Transcription	187
	Paramyxovirus : V proteins	STAT1/2	Viral modulation	188
	?	CDT1	DNA replication	67
Cul5	Adenovirus: E1B-55K, E4ORF6	p53	Viral modulation	189
	HIV: Vif	APOBEC3G	Viral modulation	190

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S3 (table) | Links between pathogens and cullin–RING ligases

Pathogen: protein	Target	Proposed mechanism of action	References
<i>Agrobacterium</i> : VirF	?	VirF F-box motif links plant protein(s) to SCF	1
Atadenoviruses: RH1/2/4/6	?	Viral F-box proteins link cellular proteins to SCF	2
Human immunodeficiency virus: Vpu	CD4	Vpu promotes degradation of CD4 by linking it to SCF ^{β-TrCP}	3
Human immunodeficiency virus: Vif	APOBEC3G	Vif SOCS/BC box links APOBEC3G to CUL5–elongin-C	4–6
Faba bean necrotic yellow virus: Clink	RB	F-box and LXCXE motifs of Clink might link RB to SCF	7
Herpes simplex virus type 1: UL9	UL9	UL9 degradation by F-box-protein NFB42 in neuronal cells	8
Human papilloma virus: E7	E7	F-box-protein SKP2 targets E7 for degradation	9
Poxvirus: BTB proteins	?	BTB domain might link cellular targets to CUL3?	10
Adenovirus: E4orf6, E1B55K	p53	E4orf6, E1B55k link p53 to elongin-BC–CUL5–RING	11,12
Paramyxovirus: SV5, HPIV2	STAT1/2	SV5, HPIV2 link STAT1/2 to DDB1–CUL4A	13
SV40: T antigen	CUL7	T antigen sequesters CUL7	14

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