Supplementary table 1. **Inactivation of E3 ubiquitin ligases by mutation**. The residues of the domain are specified in brackets. (m) indicates that the mutations were performed in the mouse version of the protein. E2: an E2-interacting residue was mutated. Zn: one of the seven cysteines or the histidine that coordinated the atoms of Zn was mutated. Catalytic cysteine: the catalytic cysteine of the HECT domain was mutated. \*specifies that the catalytic cysteine is from the RING2 domain in RBR-type E3 ligases. On each reference it is specified the substrate that was analysed.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Protein name | Uniprot Ref (human) | E3 type | Reference | Mutation | Type of mutation | Substrate |
| AMFR | [Q9UKV5](http://www.uniprot.org/uniprot/Q9UKV5) | **Ring (341-379)** | (W. Liu, Shang, and Li 2014) | A593R/F597R | **E2** |  |
| (Q. Wang et al. 2014) | C337S/C352S; C337S/C374S (m) | **Zn** | STING |
| (Ying et al. 2009) | C341G | **Zn** | SOD1; Ataxin-3 |
| ANAPC11 | [Q9NYG5](http://www.uniprot.org/uniprot/Q9NYG5) | **Ring (34-77)** | (Gmachl et al. 2000) | C51A | **Zn** | Securin; cyclin B |
| AREL1 | [O15033](http://www.uniprot.org/uniprot/O15033) | **HECT (483-823)** | (J. Bin Kim et al. 2013) | C790A | **Catalytic cysteine** | SMAC; HtrA2; ARTS |
| ARIH1 | [Q9Y4X5](http://www.uniprot.org/uniprot/Q9Y4X5) | **Ring 1 (186-236) IBR (256-317) Ring 2 (344-375)** | (Ardley et al. 2001) | C208A | **Zn** |  |
| (Duda et al. 2013) | F430A; E431A; E503A | **OTHER** |  |
| (Kelsall et al. 2013) | C357S | **Catalytic cysteine\*** |  |
| (Scott et al. 2016) | C357S | **Catalytic cysteine\*** | CRL substrates |
| (von Stechow et al. 2015) | C208A | **Zn** | 4EHP |
| (Wenzel et al. 2011) | C357S | **Catalytic cysteine\*** |  |
| ARIH2 | [O95376](http://www.uniprot.org/uniprot/O95376) | **Ring 1 (139-188) IBR (208-270) Ring 2 (297-326)** | (Kawashima et al. 2017) | C300A; H158A | **Zn** | NLRP3 |
| (Kelsall et al. 2013) | C310S | **Catalytic cysteine\*** |  |
| (Marteijn et al. 2007) | H158A | **Zn** | ¬Gf1 |
| c-IAP1 | [Q13490](http://www.uniprot.org/uniprot/Q13490) | **Ring (571-606)** | (Blankenship et al. 2009) | H588A | **Zn** | Auto |
| (Conze et al. 2005) | H582A (m) | **Zn** | c-IAP2 |
| (Li X, Yang Y, and Ashwell JD. 2002) | H588A | **Zn** | TRAF2 |
| (L. Xu et al. 2007) | H588A | **Zn** | MAD1 |
| (Y. Zhao et al. 2007) | H588A | **Zn** | ASK1 |
| c-IAP2 | [Q13489](https://www.uniprot.org/uniprot/Q13489) | **Ring (557-592)** | (Conze et al. 2005) | H570A (m) | **Zn** | Auto |
| (Conze, Zhao, and Ashwell 2010) | H570A (m) | **Zn** |  |
| (Giardino Torchia et al. 2015) | H570A (m) | **Zn** |  |
| KIAP | [Q96CA5](https://www.uniprot.org/uniprot/Q96CA5#family_and_domains) | **Ring (252-286)** | (Dou et al. 2012) | I284A | **E2** |  |
| R286A | **OTHER** |  |
| F296H | **OTHER** |  |
| V263R | **OTHER** |  |
| BMI-1 | [P35226](https://www.uniprot.org/uniprot/P35226) | **Ring (18-57)** | (Alchanati et al. 2009) | L20A | **E2** |  |
| BRAP | [Q7Z569](https://www.uniprot.org/uniprot/Q7Z569) | **Ring (264-304)** | (Hayes et al. 2012) | W295A | **E2** | Auto; USP15 |
| (Shoji et al. 2017) | C264S | **Zn** |  |
| BRCA1 | [P38398](https://www.uniprot.org/uniprot/P38398) | **Ring (24-65)** | (Eakin et al. 2007) | I26A | **E2** | ERα |
| C61G; C64G | **Zn** | ERα |
| (Fabbro and Henderson 2008) | C61G | **Zn** |  |
| C61G | **Zn** |  |
| (Morris and Solomon 2004) | C61G | **Zn** |  |
| (Nelson and Holt 2010) | C61G | **Zn** |  |
| (Nishikawa et al. 2004) | C61G | **Zn** |  |
| (Ruffner et al. 2001) | C61G; C64G; C39Y; C24R | **Zn** |  |
| T37R | **OTHER** |  |
| (Sankaran et al. 2006) | I26A | **E2** |  |
| (Stewart et al. 2017) | L63A; K65A | **OTHER** |  |
| I26A | **E2** |  |
| C61G | **Zn** |  |
| CBL | [P22681](https://www.uniprot.org/uniprot/P22681#names_and_taxonomy) | **Ring (381-420)** | (Bulut et al. 2013) | ΔY368; ΔY371 | **OTHER** | PI3K |
| (Duyvestyn et al. 2014) | C379A (m) | **Zn** |  |
| J(Javadi et al. 2013) | C384R | **Zn** |  |
| Y371H | **OTHER** |  |
| (Joazeiro et al. 1999) | W408A | **E2** | RPTKs |
| C381A | **Zn** | RPTKs |
| (Levkowitz et al. 1999) | C381A | **Zn** | EGFR |
| (Lv et al. 2017) | C381A | **Zn** | JAK2 |
| (Miura-Shimura et al. 2003) | Y700F | **OTHER** | Vav |
| (Molero et al. 2006) | C379A | **Zn** |  |
| (Oshikawa et al. 2011) | R420Q | **OTHER** | Flt3-ITD |
| (Rathinam et al. 2010) | C379A | **Zn** |  |
| (Taylor et al. 2015) | C379A | **Zn** | FLT3 |
| (Thien, Walker, and Langdon 2001) | W408A; C381A; ΔC381; H398A; ΔH398 | **Zn** | EGFR |
| Y371F; ΔY368; ΔY371 | **OTHER** | EGFR |
| (Thien et al. 2005) | C381A | **Zn** |  |
| (Waterman et al. 1999) | C381A | **Zn** | EGFR |
| (Xiong et al. 2011) | C381A | **Zn** | CSF-1R |
| CBLB | [Q13191](https://www.uniprot.org/uniprot/Q13191#sequences) | **Ring (373-412)** | (Bachmaier et al. 2007) | C373A | **Zn** |  |
| (Ettenberg et al. 2001) | C373A | **Zn** |  |
| (Oksvold et al. 2008) | C373A | **Zn** |  |
| (Oshikawa et al. 2011) | C373A | **Zn** | Flt3-ITD |
| (Rathinam et al. 2010) | C373A | **Zn** |  |
| CBLC | [Q9ULV8](https://www.uniprot.org/uniprot/Q9ULV8#sequences) | **Ring (351-390)** | (M. Kim et al. 2004) | C351A | **Zn** | SRC |
| CHFR | [Q96EP1](https://www.uniprot.org/uniprot/Q96EP1) | **Ring (304-343)** | (J. M. Kim et al. 2010) | I306A | **E2** | HLTF |
| CNOT4 | [O95628](https://www.uniprot.org/uniprot/O95628) | **Ring (14-57)** | (Albert et al. 2002) | C17A; C33R | **Zn** |  |
| L16A; I45A | **E2** |  |
| R57A | **OTHER** |  |
| DTX3L | [Q8TDB6](https://www.uniprot.org/uniprot/Q8TDB6) | **Ring (561-600)** | (Holleman and Marchese 2014) | C561A/C596A/C599A | **Zn** | CXCR4 |
| (Yong Zhang et al. 2015) | C561S; C564S | **Zn** | H2BJ |
| HACE1 | [Q8IYU2](https://www.uniprot.org/uniprot/Q8IYU2) | **HECT (574-909)** | (Anglesio et al. 2004) | C876S | **Catalytic cysteine** |  |
| (Hollstein et al. 2015) | C876S | **Catalytic cysteine** |  |
| (Palicharla and Maddika 2015) | C876S | **Catalytic cysteine** | YB-1 |
| (Torrino et al. 2011) | C876S | **Catalytic cysteine** | Rac1 |
| HECTD1 | [Q9ULT8](https://www.uniprot.org/uniprot/Q9ULT8) | **HECT(2151-2610)** | (Sarkar and Zohn 2012) | C2579G | **Catalytic cysteine** | Hsp90 |
| (Sugrue et al. 2019) | C2579G | **Catalytic cysteine** | RARA |
| (Tran et al. 2013) | C2579G | **Catalytic cysteine** | APC |
| HECTD2 | [Q5U5R9](https://www.uniprot.org/uniprot/Q5U5R9) | **HECT (437-776)** | (Coon et al. 2015) | C744S | **Catalytic cysteine** | PIAS1 |
| HECTD3 | [Q5T447](https://www.uniprot.org/uniprot/Q5T447) | **HECT (512-857)** | (Y. Li et al. 2013) | C823A | **Catalytic cysteine** | Caspase-8 |
| (F. Li et al. 2018) | C823A | **Catalytic cysteine** | TRAF3 |
| (J. Yu et al. 2008) | C539A | **Catalytic cysteine** | TARA |
| HECW2 | [Q9P2P5](https://www.uniprot.org/uniprot/Q9P2P5) | **HECT (1237-1572)** | (K. Choi et al. 2016) | C1540A | **Catalytic cysteine** | AMOTL1 |
| (Krishnamoorthy, Khanna, and Parnaik 2018) | C1540A | **Catalytic cysteine** | PCNA; lamin B1 |
| HERC2 | [O95714](https://www.uniprot.org/uniprot/O95714) | **HECT (4457-4794)** | (Chan et al. 2014) | C4762S | **Catalytic cysteine** | USP33 |
| (Kühnle et al. 2011) | C4762S | **Catalytic cysteine** |  |
| (Wu et al. 2010) | C4762S | **Catalytic cysteine** | BRCA1 |
| HERC3 | [Q15034](https://www.uniprot.org/uniprot/Q15034) | **HECT (951-1050)** | (Cruz et al. 2001) | C1018A | **Catalytic cysteine** |  |
| (Hochrainer et al. 2015) | C1018A | **Catalytic cysteine** | RelA |
| HERC5 | [Q9UII4](https://www.uniprot.org/uniprot/Q9UII4) | **HECT (702-1024)** | (Kroismayr et al. 2004) | C994A | **Catalytic cysteine** |  |
| (Shi et al. 2010) | C994A | **Catalytic cysteine** | IRF3 |
| (Wong et al. 2006) | C994A | **Catalytic cysteine** |  |
| HUWE1 | [Q7Z6Z7](https://www.uniprot.org/uniprot/Q7Z6Z7) | **HECT (4038-4374)** | (Y.-F. Cheng, Tong, and Edge 2016) | C4341A | **Catalytic cysteine** | Atoh1 |
| (de Groot et al. 2014) | C4341A | **Catalytic cysteine** | Dvl |
| (Forget et al. 2014) | C4341A | **Catalytic cysteine** | Atoh1 |
| (Kurokawa et al. 2013) | C4341A | **Catalytic cysteine** | Mcl-1; PP5 |
| (Xiaozhen Wang et al. 2014) | C4341A | **Catalytic cysteine** | BRCA1 |
| (X. Zhao et al. 2008) | C4341S | **Catalytic cysteine** | N-Myc |
| Itch | [Q96J02](https://www.uniprot.org/uniprot/Q96J02) | **HECT (569-903)** | (Angers, Ramjaun, and McPherson 2004) | C830A | **Catalytic cysteine** | Endophilin A1 |
| (Chmura et al. 2017) | C830A | **Catalytic cysteine** | vFLIP |
| (Han et al. 2016) | C830A | **Catalytic cysteine** | VP40 |
| (Theivanthiran et al. 2015) | C830A | **Catalytic cysteine** | Tab1 |
| LNX1 | [Q8TBB1](https://www.uniprot.org/uniprot/Q8TBB1) | **Ring (41-79)** | (Lenihan, Saha, and Young 2017) | C48A (m) | **Zn** | PPFIA1; KLHL11; KIF7; ERC2 |
| (Nie et al. 2002) | C45A (m) | **Zn** | Numb |
| (Wolting et al. 2011) | C45A (m) | **Zn** | Numb |
| MARCH2 | [Q9P0N8](https://www.uniprot.org/uniprot/Q9P0N8) | **RING (56-116)** | (J. Cheng and Guggino 2013) | C64S/C67S | **Zn** | CFTR |
| MARCH5 | [Q9NX47](https://www.uniprot.org/uniprot/Q9NX47) | **Ring (6-75)** | (Z. Chen et al. 2017) | H43W; C65S; C68S | **Zn** | FUNDC1 |
| (Karbowski, Neutzner, and Youle 2007) | H43W; C65S; C68S | **Zn** | Drn1 |
| (Y. Y. Park et al. 2010) | H43W | **Zn** | Mfn1 |
| (Yoo et al. 2015) | H43W | **Zn** | MAVS |
| MARCH6 | [O60337](https://www.uniprot.org/uniprot/O60337) | **Ring (1-62)** | (Zattas et al. 2016) | C9A; C39S | **Zn** |  |
| MARCH8 | [Q5T0T0](https://www.uniprot.org/uniprot/Q5T0T0) | **Ring (72-133)** | (R. Chen et al. 2012) | W114A | **E2** | IL1RAP |
| MARCH9 | [Q86YJ5](https://www.uniprot.org/uniprot/Q86YJ5) | **Ring (102-162)** | (Hör et al. 2009) | W143A | **E2** | FcγRIIb; SLAM |
| (Tan et al. 2019) | W143A | **E2** | HLA-A2 |
| MDM2 | [Q00987](https://www.uniprot.org/uniprot/Q00987) | **Ring (438-479)** | (Bonacci et al. 2017) | C462A | **Zn** | NUB1 |
| (Boyd, Tsai, and Jacks 2000) | C464A | **Zn** | p53 |
| (Brenkman et al. 2008) | C464A | **Zn** | FOXO4 |
| (C. Fan and Wang 2017) | L468A | **E2** | p53 |
| (Fang et al. 2000) | C464A; C461S; C478S; C475G; H452A; H457S; T455A | **Zn** | p53 |
| (Geyer, Yu, and Maki 2000) | C464A | **Zn** | p53 |
| (Gopinathan et al. 2009) | C464A | **Zn** | PPARα |
| (He et al. 2013) | C464A | **Zn** |  |
| (Honda and Yasuda 2000) | C464A; C441A; C449A; C461A; C475A; C478A; C439A | **Zn** | Auto; p53 |
| (Honda, Tanaka, and Yasuda 1997) | C464A | **Zn** | p53 |
| (Inuzuka et al. 2010) | C464A | **Zn** |  |
| (Kannemeier, Liao, and Sun 2007) | C436L; H455S; C459S; C473G | **E2** | p53 |
| (Kawai, Wiederschain, and Yuan 2003) | C464A | **Zn** | p53 |
| (Kubbutat et al. 1999) | C464A | **Zn** | p53 |
| (Linke et al. 2008) | L468A; I440A; P476A | **E2** | Auto; Mdm4 |
| R479A | **OTHER** | Auto; Mdm4 |
| (Nomura et al. 2017) | I440E,K | **E2** | p53 |
| R479P | **OTHER** | p53 |
| (Pettersson et al. 2009) | C464A | **Zn** | IRF-2 |
| (Poyurovsky et al. 2007) | F490Q | **OTHER** |  |
| (Tian et al. 2017) | C462A | **Zn** | p53 |
| (Uchida et al. 2005) | C438A | **Zn** | pRb |
| (Wawrzynow et al. 2009) | C464A; C478S | **Zn** | p53 |
| MDM4 | [O15151](https://www.uniprot.org/uniprot/O15151) | **Ring (437-478)** | (Egorova and Sheng 2014) | T459A; K478R; S438V/E441Q; T459A/H462T; R453/K478R | **E2** | Auto |
| MEX3C | [Q5U5Q3](https://www.uniprot.org/uniprot/Q5U5Q3) | **Ring (608-648)** | (Kuniyoshi et al. 2014) | C601A (m) | **Zn** | RIG-I |
| MGRN1 | [O60291](https://www.uniprot.org/uniprot/O60291) | **Ring (278-317)** | (Benvegnù, Wahle, and Dotti 2017) | C278A; C281A | **Zn** | APP |
| (Gunn et al. 2013) | C278A; C281A | **Zn** | TSG101 |
| (Jiao et al. 2009) | C278A; C281A | **Zn** | TSG101 |
| MIB2 | [Q96AX9](https://www.uniprot.org/uniprot/Q96AX9) | **Ring 1 (890-925) Ring 2 (969-1002)** | (Ye et al. 2014) | C983S | **Catalytic cysteine\*** | MAVS |
| MID1 | [O15344](https://www.uniprot.org/uniprot/O15344) | **Ring (10-60) B-BOX1 (115-165) B-BOX2 (172-212)** | (H. Du et al. 2013) | L146Q | **OTHER** | α4 |
| MKRN1 | [Q9UHC7](https://www.uniprot.org/uniprot/Q9UHC7) | **Ring (281-335)** | (J. H. Kim et al. 2005) | H307E | **Zn** | hTERT |
| (Ko et al. 2010) | H307E | **Zn** | WNVCp |
| (E. Lee et al. 2009) | H307E | **Zn** | p53; p21 |
| (M. S. Lee et al. 2018) | H307E | **Zn** | AMPK |
| MUL1 | [Q969V5](https://www.uniprot.org/uniprot/Q969V5) | **Ring (302-340)** | (Zemirli et al. 2014) | C339A | **Zn** |  |
| MYLIP (IDOL) | [Q8WY64](https://www.uniprot.org/uniprot/Q8WY64) | **Ring (387-422)** | (J. Gao et al. 2017) | C387A | **Zn** | ApoER2 |
| (Hong et al. 2010) | C387A | **Zn** | VLDLR; ApoER2 |
| (Sorrentino et al. 2011)  | C387A | **Zn** | LDLR |
| (Zelcer et al. 2009) | C387A | **Zn** | LDLR |
| NEDD4 | [P46934](https://www.uniprot.org/uniprot/P46934) | **HECT (984-1318)** | (Q. Lin et al. 2017) | C867A | **Catalytic cysteine** | SQSTM1 |
| (F. Song et al. 2013) | C967S | **Catalytic cysteine** | THO |
| (Sugeno et al. 2014) | C867A | **Catalytic cysteine** | α-Synuclein |
| (Xinjiang Wang et al. 2008) | C967S | **Catalytic cysteine** | PTEN |
| (Zeng et al. 2014) | C867A | **Catalytic cysteine** | PTEN |
| NEDD4L | [Q96PU5](https://www.uniprot.org/uniprot/Q96PU5) | **HECT (640-974)** | (Albesa et al. 2011) | C801S | **Catalytic cysteine** | hERG1 |
| (Arroyo et al. 2011) | C822S (m) | **Catalytic cysteine** | NCC |
| (Debonneville et al. 2001) | C962A | **Catalytic cysteine** | ENaC |
| (Ding et al. 2013) | C821A | **Catalytic cysteine** | Dvl2 |
| (S. Gao et al. 2009) | C962A | **Catalytic cysteine** | Smad2; Smad3 |
| (Y. H. Kim et al. 2018) | C942A (m) | **Catalytic cysteine** | CRTC3 |
| (Palmada et al. 2004) | C938S | **Catalytic cysteine** | NaPi Iib |
| (D. Xu et al. 2016) | C821A | **Catalytic cysteine** | hOAT1 |
| (R. Zhou, Patel, and Snyder 2007) | C821A | **Catalytic cysteine** | Auto |
| C821A | **Catalytic cysteine** | α-,β-, γENaC |
| PJA2 | [O43164](https://www.uniprot.org/uniprot/O43164) | **Ring (634-675)** | (Faust et al. 2017) | C634A/C671A | **Zn** | Tat |
| PRKN | [O60260](https://www.uniprot.org/uniprot/O60260) | **Ring 0 (141-225) Ring 1 (238-293) Ring 2 ( 418-449)** | (Aguileta et al. 2015) | C431F | **Catalytic cysteine\*** |  |
| (Ahmed et al. 2011) | G430D; T415N | **OTHER** | Arrestin-3 |
| (Bendikov-Bar et al. 2014) | T240R | **OTHER** | Gcase; PARIS; ARTS |
| (D. Chen et al. 2010) | C431F | **Catalytic cysteine\*** | Bcl-2 |
| K161N; T240R; P437L | **OTHER** | Bcl-2 |
| (Fiesel et al. 2015) | C431S | **Catalytic cysteine\*** |  |
| (Joch et al. 2007) | C431F | **Catalytic cysteine\*** | PICK1 |
| (Johnson et al. 2012) | R275W; W453X | **OTHER** | Bax |
| (Juan Liu et al. 2017) | C431A | **Catalytic cysteine\*** | HIF-1 |
| (Matteucci et al. 2018) | G430D | **OTHER** | MICU1 |
| (McWilliams et al. 2018) | C431S | **Catalytic cysteine\*** |  |
| (Moore et al. 2008) | T240R | **OTHER** | Hsp70 |
| (Riley et al. 2013) | C431S, A | **Catalytic cysteine\*** |  |
| (Sarraf et al. 2013) | C431F | **Catalytic cysteine\*** |  |
| (P. Song et al. 2016) | C431S | **Catalytic cysteine\*** | Rab7 |
| (Y. Wang et al. 2018) | K151E | **OTHER** | RIPK1 |
| (Wauer et al. 2015) | K151E | **OTHER** |  |
| (Xin et al. 2018) | C431S | **Catalytic cysteine\*** | TRAF3 |
| RAD18 | [Q9NS91](https://www.uniprot.org/uniprot/Q9NS91) | **Ring (25-64)** | (J. Huang et al. 2009) | C28F | **Zn** |  |
| (Masuda et al. 2012) | I50A/R51A | **E2** |  |
| (Tateishi et al. 2000) | C28F | **Zn** |  |
| (Williams et al. 2011) | C28F | **Zn** | FANCD2 |
| RAG1 | [P15918](https://www.uniprot.org/uniprot/P15918) | **(Ring 293-332)** | (Jones and Gellert 2003) | C328Y | **Zn** | Auto |
| RC3H2 | [Q9HBD1](https://www.uniprot.org/uniprot/Q9HBD1) | **Ring (14-54)** | (Maruyama et al. 2014) | C33S | **Zn** | ASK1 |
| RFFL | [Q8WZ73](https://www.uniprot.org/uniprot/Q8WZ73) | **Ring (316-351)** | (Sakai et al. 2019) | C316A/C319A; H333A | **Zn** | Rab11 effectors |
| RFWD3 | [Q6PCD5](https://www.uniprot.org/uniprot/Q6PCD5) | **Ring (287-331)** | (Feeney et al. 2017) | C315A | **Zn** |  |
| Ring1 | [Q06587](https://www.uniprot.org/uniprot/Q06587) | **Ring (48-88)** | (Shen et al. 2018) | I50A | **E2** | p53 |
| RLIM | [Q9NVW2](https://www.uniprot.org/uniprot/Q9NVW2) | **Ring (570-611)** | (R. Gao, Wang, et al. 2016) | C596A | **Zn** | c-Myc |
| RNF125 | [Q96EQ8](https://www.uniprot.org/uniprot/Q96EQ8) | **Ring (37-76)** | (Jia et al. 2017) | C72A/C75A | **Zn** | TRIM14 |
| (L. Yang et al. 2015) | C72A/C75A | **Zn** | p53 |
| RNF126 | [Q9BV68](https://www.uniprot.org/uniprot/Q9BV68) | **Ring (229-270)** | (Benini et al. 2017) | C229A/C232A | **Zn** | Frataxin |
| RNF138 | [Q8WVD3](https://www.uniprot.org/uniprot/Q8WVD3) | **Ring (18-58)** | (W. Kim et al. 2018) | C18A/C54A | **Zn** | rpS3 |
| RNF144A | [P50876](https://www.uniprot.org/uniprot/P50876) | **Ring 1 (20-70) IBR (91-156) Ring 2 atypical (185-214)** | (Ye Zhang et al. 2017) | C20A/C23A | **Zn** | PARP1 |
| (Ho et al. 2014) | C20A/C23A | **Zn** | DNA-PKcs |
| RNF145 | [Q96MT1](https://www.uniprot.org/uniprot/Q96MT1) | **Ring (537-575)** | (Jiang et al. 2018) | C537A | **Zn** | HMGCR |
| (Menzies et al. 2018) | C552A/H554A | **Zn** | HMGCR |
| RNF146 | [Q9NTX7](https://www.uniprot.org/uniprot/Q9NTX7) | **Ring (37-75)** | (Callow et al. 2011) | H53A | **Zn** | Axin; Tankyrase |
| RNF152 | [Q8N8N0](https://www.uniprot.org/uniprot/Q8N8N0) | **Ring (12-55)** | (Deng et al. 2015) | 4C-->S | **Zn** | RagA GTPase |
| RNF167 | [Q9H6Y7](https://www.uniprot.org/uniprot/Q9H6Y7) | **Ring (230-272)** | (Deshar et al. 2016) | C233S | **Zn** | Arl8B |
| RNF168 | [Q8IYW5](https://www.uniprot.org/uniprot/Q8IYW5) | **Ring (16-55)** | (Pinato et al. 2009) | C16S/C19S | **Zn** | H2A; H2AX |
| RNF185 | [Q96GF1](https://www.uniprot.org/uniprot/Q96GF1) | **Ring (39-80)** | (El Khouri et al. 2013) | C39A/C42A | **Zn** | CFTR |
| RNF2 | [Q99496](https://www.uniprot.org/uniprot/Q99496) | **Ring (51-91)** | (S. Liu et al. 2018) | I53A | **E2** | H2A |
| (Xia et al. 2014) | H69Y | **Zn** | AMBRA1 |
| RNF220 | [Q6PDX6](https://www.uniprot.org/uniprot/Q6PDX6) | **Ring (513-553)** | (Ma et al. 2014) | W539R | **E2** | Sin3B |
| RNF25 | [Q96BH1](https://www.uniprot.org/uniprot/Q96BH1) | **Ring (134-203)** | (R. Gao, Ma, et al. 2016) | C135A/C138A | **Zn** |  |
| RNF26 | [Q9BY78](https://www.uniprot.org/uniprot/Q9BY78) | **Ring (378-425)** | (Qin et al. 2014) | C395S; C399S; C401S | **Zn** | STING |
| RNF31 | [Q96EP0](https://www.uniprot.org/uniprot/Q96EP0) | **Ring 1 (699-749)IBR (779-841) Ring 2 (871-901)** | (Smit et al. 2012) | C871A/C874A; C890A/C893A; C885A/H887A; C898A/C901A; C719A; C885A/H887A; C885S | **Zn** |  |
| (Zhu et al. 2018) | C871A/C874A; C890A/C893A; C885A/H887A; C898A/C901A; C719A; C885A/H887A; C885S | **Zn** | FOXP3 |
| RNF34 | [Q969K3](https://www.uniprot.org/uniprot/Q969K3) | **Ring (325-360)** | (H. Jin et al. 2014) | H342A | **Zn** | GABAARs |
| (Wei et al. 2018) | C656A (d) | **Zn** | PGC-1 |
| (R. Zhang et al. 2014) | H342A | **Zn** | NOD-1 |
| RNF4 | [P78317](https://www.uniprot.org/uniprot/P78317) | **Ring (132-177)** | (Liew et al. 2010) | M149A; D141A; V161A; V134E; S155E R181A; Y193A (m) | **OTHER** |  |
| RNF40 | [O75150](https://www.uniprot.org/uniprot/O75150) | **Ring (948-987)** | (Foglizzo, Middleton, and Day 2016) | Y999A | **OTHER** |  |
| RNF43 | [Q68DV7](https://www.uniprot.org/uniprot/Q68DV7) | **Ring (272-313)** | (Loregger et al. 2015) | H292R | **Zn** | TCF4 |
| RNF8 | [O76064](https://www.uniprot.org/uniprot/O76064) | **Ring (403-441)** | (Lu et al. 2012) | C403S | **Zn** | Nsb1 |
| (Mailand et al. 2007) | C403S | **Zn** | H2A; H2AX |
| (Mallette et al. 2012) | I405A | **E2** | JMJD2A |
| (Rai et al. 2011) | C406S | **Zn** | TPP1 |
| (Tripathi and Smith 2017) | C403S | **Zn** | TNKS1 |
| SHPRH | [Q149N8](https://www.uniprot.org/uniprot/Q149N8) | **Ring (1432-1479)** | (Motegi et al. 2006) | C1432A | **Zn** | PCNA |
| SIAH1 | [Q8IUQ4](https://www.uniprot.org/uniprot/Q8IUQ4) | **Ring (41-76)** | (Grishina et al. 2012) | C44S | **Zn** | CBP/p300 |
| (Ji et al. 2017) | C41S/C44S (m) | **Zn** | Axin 1 |
| (Se-yong Kim et al. 2009) | C41S/C44S (m) | **Zn** | HIPK2 |
| (S. Lee et al. 2015) | C44S | **Zn** | p34 |
| (M. Liu et al. 2012) | C75S | **Zn** | ELL2 |
| (Pietschmann et al. 2012) | C72S | **Zn** | PML-RARα |
| (Y. Zhou et al. 2008) | C41S/C44S (m) | **Zn** | TRB3 |
| SIAH2 | [O43255](https://www.uniprot.org/uniprot/O43255) | **Ring (80-115)** | (Habelhah et al. 2002) | H99A/C102A (m) | **Zn** | TRAF2 |
| SMURF1 | [Q9HCE7](https://www.uniprot.org/uniprot/Q9HCE7) | **HECT (420-757)** | (Fei et al. 2013) | C699A (m) | **Catalytic cysteine** | Axin |
| (Shan Li et al. 2010) | C699A (m) | **Catalytic cysteine** | TRAF4 |
| (Tajima et al. 2003) | I612A/L614A (m) | **OTHER** | Smad7 |
| (H.-R. Wang et al. 2006) | C699A (m) | **Catalytic cysteine** |  |
| (Xiangchun Wang et al. 2013) | C710A | **Catalytic cysteine** | TRAF4 |
| (M. Zhao et al. 2003) | C710A | **Catalytic cysteine** | Smad1; Cbfa1 |
| SMURF2 | [Q9HAU4](https://www.uniprot.org/uniprot/Q9HAU4) | **HECT (414-748)** | (Borroni et al. 2018) | C716G | **Catalytic cysteine** | Lamin A |
| (J. X. Du et al. 2011) | C716A | **Catalytic cysteine** | KLF5 |
| (Jeong et al. 2014) | C716G | **Catalytic cysteine** | YY1 |
| (C. Jin et al. 2009) | C716G | **Catalytic cysteine** |  |
| (Sewoon Kim and Jho 2010) | C716G | **Catalytic cysteine** | Axin |
| (Pan et al. 2014) | C716A | **Catalytic cysteine** | MAVS |
| (Shukla et al. 2014) | C716A | **Catalytic cysteine** | KRAS |
| STUB1 | [Q9UNE7](https://www.uniprot.org/uniprot/Q9UNE7) | **U-BOX (226-300)** | (M. Fan, Park, and Nephew 2005) | H260Q | **E2** | Erα |
| (J.-H. Kim et al. 2017) | H260Q | **E2** | PPARγ |
| (X. Li et al. 2018) | H260Q | **E2** | IRS4 |
| P269A | **E2** | IRS4 |
| (Seo et al. 2018) | H260Q | **E2** | SNPH |
| (Shimamoto et al. 2013) | H260Q | **E2** |  |
| P269A | **E2** |  |
| SYVN1 | [Q86TM6](https://www.uniprot.org/uniprot/Q86TM6) | **Ring (291-330)** | (Tanabe et al. 2012)  | C307A | **Zn** | RER1 |
| TRAF6 | [Q9Y4K3](https://www.uniprot.org/uniprot/Q9Y4K3) | **Ring (70-109)** | (Y. B. Choi and Harhaj 2014) | C70A | **Zn** | Mcl-1 |
| (Funakoshi-Tago et al. 2009) | C70A | **Zn** |  |
| (Ning et al. 2008) | C70A | **Zn** | IRF7 |
| (W. L. Yang et al. 2009) | C70A | **Zn** | Akt |
| (Jiazhen Zhang et al. 2017) | C70A | **Zn** |  |
| L74H | **E2** |  |
| TRIM11 | [Q96F44](https://www.uniprot.org/uniprot/Q96F44) | **Ring (16-57) B-BOX (87-128)** | (L. Chen et al. 2018) | C16A/C19A | **Zn** |  |
| (T. Liu et al. 2016) | C53A7 C56A | **Zn** | AIM2 |
| TRIM13 | [O60858](https://www.uniprot.org/uniprot/O60858) | **Ring (10-58) B-BOX (89-131)** | (B. Huang et al. 2018) | C10A/C13A | **Zn** | Nur77 |
| TRIM17 | [Q9Y577](https://www.uniprot.org/uniprot/Q9Y577) | **Ring (16-66) B-BOX (94-135)** | (Lassot et al. 2010) | C16A | **Zn** |  |
| TRIM21 | [P19474](https://www.uniprot.org/uniprot/P19474) | **Ring (16-55) B-BOX (92-123)** | (Wada and Kamitani 2006) | C16A | **Zn** | p62 |
| TRIM22 | [Q8IYM9](https://www.uniprot.org/uniprot/Q8IYM9) | **Ring (15-60) B-BOX (92-133)** | (Duan et al. 2008) | C15A | **Zn** | Auto |
| TRIM23 | [P36406](https://www.uniprot.org/uniprot/P36406) | **Ring (31-76) B-BOX (122-168)** | (Arimoto et al. 2010) | C34A | **Zn** | NEMO |
| (Sparrer et al. 2017) | C34A | **Zn** |  |
| TRIM25 | [Q14258](https://www.uniprot.org/uniprot/Q14258) | **Ring (13-54)** | (J. M. Lee et al. 2018) | C50S/C53S | **Zn** | PPARγ |
| TRIM26 | [Q12899](https://www.uniprot.org/uniprot/Q12899) | **Ring (16-57) B-BOX (97-138)** | (Ran et al. 2016) | C31S | **Zn** |  |
| TRIM27 | [P14373](https://www.uniprot.org/uniprot/P14373) | **Ring (16-57) B-BOX (96-127)** | (Zaman et al. 2013) | C96A/C99A/H107A/D110A | **Zn** | USP7 |
| (Zurek et al. 2012) | C16A/C31A | **Zn** | NOD2 |
| TRIM3 | [O75382](https://www.uniprot.org/uniprot/O75382) | **Ring (22-63) B-BOX (110-151)** | (Hung et al. 2010) | C22A/C25A | **Zn** | GKAP/SAPAP1 |
| (Raheja et al. 2014) | C22A/C25A | **Zn** | p21 |
| I24A; L26A; D27A; V61A; R63A | **E2** | p21 |
| TRIM31 | [Q9BZY9](https://www.uniprot.org/uniprot/Q9BZY9) | **Ring (16-57) B-BOX (90-131)** | (B. Liu et al. 2017) | C53A/C56A | **Zn** | MAVS |
| (H. Song et al. 2016) | C16A/C36A | **Zn** | NLRP3 |
| TRIM32 | [Q13049](https://www.uniprot.org/uniprot/Q13049) | **Ring (20-65) B-BOX (103-133)** | (Fu et al. 2015) | C39S | **Zn** | PB1 |
| (Koliopoulos et al. 2016) | E16R | **OTHER** |  |
| (Ryu et al. 2011) | C23A | **Zn** | XIAP |
| (Jing Zhang et al. 2012) | C39S | **Zn** | STING |
| TRIM33 | [Q9UPN9](https://www.uniprot.org/uniprot/Q9UPN9) | **Ring (125-154) B-BOX1 (212-259) B-BOX2 (271-312)** | (Xue et al. 2015) | C125A/C128A | **Zn** | β-catenin |
| TRIM37 | [O94972](https://www.uniprot.org/uniprot/O94972) | **Ring (15-55) B-BOX (90-132)** | (Bhatnagar et al. 2014) | C18R | **Zn** | H2A |
| (Kallijärvi et al. 2005) | C35S/C36S | **Zn** |  |
| (W. Wang et al. 2017) | C35S/C36S; C18R | **Zn** | PEX5 |
| TRIM4 | [Q9C037](https://www.uniprot.org/uniprot/Q9C037) | **Ring (12-53) B-BOX (82-123)** | (J. Yan et al. 2014) | C27S | **Zn** | RIG-1 |
| TRIM45 | [Q9H8W5](https://www.uniprot.org/uniprot/Q9H8W5) | **Ring (29-98) B-BOX1 (130-176) B-BOX2 (186-227)** | (Jindong Zhang et al. 2017) | C29A | **Zn** | p53 |
| TRIM49 | [P0CI25](https://www.uniprot.org/uniprot/P0CI25) | **Ring (15-56) B-BOX (88-129)** | (Guimarães and Gomes 2018) | C35S | **Zn** |  |
| TRIM5 | [Q9C035](https://www.uniprot.org/uniprot/Q9C035) | **Ring (15-59) B-BOX (90-132)** | (Lienlaf et al. 2011) | R60A | **E2** | Auto |
| (Yamauchi et al. 2008) | C15A | **Zn** |  |
| (Yudina et al. 2015) | Y63E; I77R | **OTHER** |  |
| TRIM50 | [Q86XT4](https://www.uniprot.org/uniprot/Q86XT4) | **Ring (16-57) B-BOX (84-125)** | (Fusco et al. 2012) | C52X (m) | **Zn** |  |
| TRIM6 | [Q9C030](https://www.uniprot.org/uniprot/Q9C030) | **Ring (15-60) B-BOX (92-133)** | (Bharaj et al. 2017) | C15A | **Zn** | VP35 |
| TRIM62 | [Q9BVG3](https://www.uniprot.org/uniprot/Q9BVG3) | **Ring (11-54) B-BOX (88-128)** | (Zhifang Cao et al. 2015) | C11A/C14A | **Zn** | CARD9 |
| (F. Huang et al. 2013) | C11A | **Zn** |  |
| TRIM65 | [Q6PJ69](https://www.uniprot.org/uniprot/Q6PJ69) | **Ring (12-51) B-BOX (90-137)** | (Shitao Li et al. 2014) | C12A/C15A | **Zn** | TNRC6 |
| TRIM7 | [Q9C029](https://www.uniprot.org/uniprot/Q9C029) | **Ring (29-82) B-BOX (125-166)** | (Chakraborty et al. 2015) | C29A/C32A | **Zn** | RACO-1 |
| W57A | **E2** | RACO-1 |
| TRIM71 | [Q2Q1W2](https://www.uniprot.org/uniprot/Q2Q1W2) | **Ring (12-95) B-BOX 1 (194-241) B-BOX2 (273-314)** | (Yin et al. 2016) | C12A/C15A | **Zn** | Lin28B |
| TRIM8 | [Q9BZR9](https://www.uniprot.org/uniprot/Q9BZR9) | **Ring (15-56) B-BOX1 (92-132) B-BOX2 (140-182)** | (F.-J. Yan et al. 2017) | C15A/C18A | **Zn** | TAK1 |
| TRIP12 | [Q14669](https://www.uniprot.org/uniprot/Q14669) | **HECT (1885-1992)** | (Hanoun et al. 2014) | C1959A | **Catalytic cysteine** | PTF1a |
| (Y. Park, Yoon, and Yoon 2009) | C1972S | **Catalytic cysteine** |  |
| UBE3A | [Q05086](https://www.uniprot.org/uniprot/Q05086) | **HECT (776-875)** | (Chhabra et al. 2017) | C843A | **Catalytic cysteine** | G-CSFR |
| (Harlalka et al. 2013) | C820A | **Catalytic cysteine** |  |
| (Kumar, Talis, and Howley 1999) | C833A | **Catalytic cysteine** | HHR23 |
| (S. Y. Lee et al. 2014) | C941S (d) | **Catalytic cysteine** | Rpn10 |
| (Mortensen et al. 2015) | C820A | **Catalytic cysteine** |  |
| (Munakata et al. 2007) | C840A | **Catalytic cysteine** | pRb |
| (Pal et al. 2013) | C843A | **Catalytic cysteine** | C/EBPα |
| (Y. Yang et al. 2007) | C833A | **Catalytic cysteine** | TH1 |
| UBE3C | [Q15386](https://www.uniprot.org/uniprot/Q15386) | **HECT (744-1083)** | (Chu et al. 2013) | C1051A | **Catalytic cysteine** |  |
| (Y. Yu and Hayward 2010) | C1051A | **Catalytic cysteine** | IRF3; IRF7 |
| UBE4B | [O95155](https://www.uniprot.org/uniprot/O95155) | **U-BOX (1227-1300)** | (Okumura et al. 2004) | P1140A (m) | **OTHER** | FEZ1 |
| UBR1 | [Q8IWV7](https://www.uniprot.org/uniprot/Q8IWV7) | **Ring (1098-1201)** | (Sasaki et al. 2006) | C1098S | **Zn** | c-FOS |
| UBR5 | [O95071](https://www.uniprot.org/uniprot/O95071) | **HECT (2462-2799)** | (T. Zhang et al. 2014) | C2768A | **Catalytic cysteine** | ATMIN |
| UHRF1 | [Q96T88](https://www.uniprot.org/uniprot/Q96T88) | **Ring (724-763)** | (Nishiyama et al. 2013) | C713A/C715A/C716A (m) | **Zn** | H3 |
| (H. Zhang et al. 2016) | H754A | **Zn** | RIF-1 |
| WWP1 | [Q9H0M0](https://www.uniprot.org/uniprot/Q9H0M0) | **HECT (588-922)** | (Han et al. 2017) | C890A | **Catalytic cysteine** | VP40 |
| (Heidecker et al. 2007) | C890S | **Catalytic cysteine** | Gag |
| (Laine and Ronai 2007) | C883A | **Catalytic cysteine** | p53 |
| (L. Lin et al. 2016) | C886S (m) | **Catalytic cysteine** | Htt (160Q) |
| (Zaarour et al. 2012) | C890A | **Catalytic cysteine** | Ezrin |
| (Z. Zhou, Liu, and Chen 2012) | C890A | **Catalytic cysteine** |  |
| WWP2 | [O00308](https://www.uniprot.org/uniprot/O00308) | **HECT (536-870)** | (Jung et al. 2014) | C838A | **Catalytic cysteine** | Notch3 |
| (Luo et al. 2014) | C838A | **Catalytic cysteine** | SRG3 |
| (Nakamura et al. 2011) | C838A | **Catalytic cysteine** | Sox9 |
| (H. M. Xu et al. 2004) | C838A | **Catalytic cysteine** | oct-04 |
| XIAP | [P98170](https://www.uniprot.org/uniprot/P98170) | **Ring (450-485)** | (Zipeng Cao et al. 2013) | H467A | **Zn** | Cyclin D1 |
| (Jinyi Liu et al. 2012) | H467A | **Zn** |  |
| (Nakatani et al. 2013) | F495A; F495L; V461E | **OTHER** |  |
| (Q. Yang 2004) | H467A | **Zn** | Auto |
| ZNRF1 | [Q8ND25](https://www.uniprot.org/uniprot/Q8ND25) | **Ring (184-225)** | (Toshiyuki and Milbrandt 2003) | C184A | **Zn** |  |
| ZNRF2 | [Q8NHG8](https://www.uniprot.org/uniprot/Q8NHG8) | **Ring (199-240)** | (Toshiyuki and Milbrandt 2003) | C199A | **Zn** |  |
| ZNRF4 | [Q8WWF5](https://www.uniprot.org/uniprot/Q8WWF5) | **Ring (309-352)** | (Bist et al. 2017) | H329W/H332W | **Zn** | RIP2 |

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