(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
12 May 2022 (12.05.2022)

WIPO | PCT

(10) International Publication Number
WO 2022/099038 A1

(51) International Patent Classification:
C07K 14/415 (2006.01) *C12N 15/86* (2006.01)
C12N 9/22 (2006.01)

(21) International Application Number:
PCT/US2021/058291

(22) International Filing Date:
05 November 2021 (05.11.2021)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/110,619 06 November 2020 (06.11.2020) US

(71) Applicant: **PETRICHOR HEALTHCARE CAPITAL MANAGEMENT LP** [US/US]; 885 Third Avenue, 24th Floor, New York, New York 10022 (US).

(72) Inventors: **LOEW, Andreas**; 47 Cove Street, Mattapoisett, Massachusetts 02739 (US). **HALL, Samuel W.**; 150 N 5th Street, Apt. 3K, Brooklyn, New York 11211 (US).

(74) Agent: **GRANT, Angela M.**; LathropGPM, 28 State Street, 7th Floor, Boston, Massachusetts 02109 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,

(54) Title: MEMBRANE PROTEIN TARGETING ENGINEERED DEUBIQUITINASES AND METHODS OF USE THEREOF

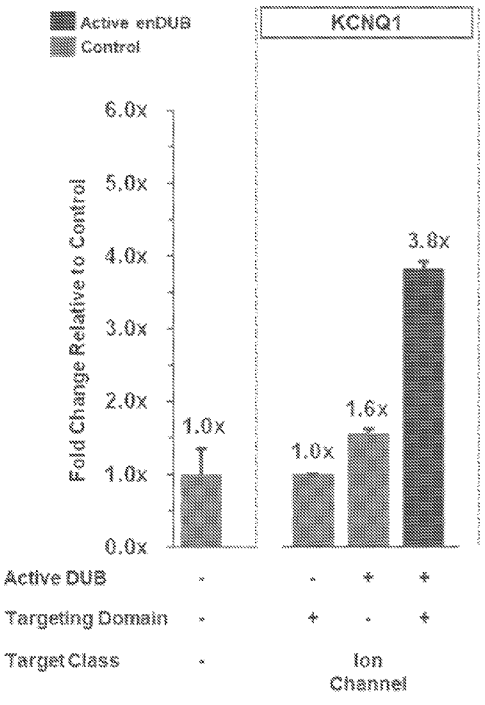


FIG. 3

(57) Abstract: Provided herein are fusion protein comprising: an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof; and a targeting domain comprising a moiety that specifically binds a membrane protein. Also provided herein are methods of using the fusion proteins to treat a disease, including genetic diseases.

WO 2022/099038 A1

[Continued on next page]

TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

MEMBRANE PROTEIN TARGETING ENGINEERED DEUBIQUITINASES AND METHODS OF USE THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Patent Application No. 63/110,619, filed November 6, 2020, the entire disclosure of which is incorporated herein by reference.

1. FIELD

[0001] This disclosure relates to fusion proteins comprising an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof; and a targeting domain comprising a moiety that specifically binds a target membrane protein. The disclosure further relates to therapeutic methods of using the same.

2. BACKGROUND

[0002] A subset of genetic diseases are associated with a decrease in the level of expression of a functional membrane protein or a decrease in the stability of a membrane protein. For example, haploinsufficiency genetic diseases are caused by the presence a single copy of a wild-type allele in heterozygous combination with a loss of function variant allele, wherein the level of functional protein expressed is insufficient to produce the standard phenotype. Haploinsufficiency can arise from a de novo or inherited loss-of-function mutation in the variant allele, such that it produces little or no functional protein. Despite recent developments in gene therapy, there are still no curative treatments for these diseases, and treatment typically centers on the management of symptoms. Therefore, new treatments are needed for diseases, e.g., genetic diseases, that are associated with decreased functional membrane protein expression or stability.

3. SUMMARY

[0003] Provided herein are, *inter alia*, engineered deubiquitinases (enDubs) that comprise a targeting moiety that specifically binds a membrane target protein and a catalytic domain of a deubiquitinase. The targeting moiety directs that deubiquitinase catalytic domain to the specific target membrane protein for deubiquitination. The fusion proteins described herein are particularly useful in methods of treating genetic diseases, particularly those associated with or caused by

decreased expression or stability of a specific membrane protein.

[0004] In one aspect, provided herein are fusion proteins comprising: an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof; and a targeting domain comprising a targeting moiety that specifically binds a membrane protein that is not an ion channel.

[0005] In some embodiments, the deubiquitinase is a cysteine protease or a metalloprotease.

[0006] In some embodiments, the deubiquitinase is a cysteine protease. In some embodiments, the cysteine protease is a ubiquitin-specific protease (USP), a ubiquitin C-terminal hydrolase (UCH), a Machado-Josephin domain protease (MJD), an ovarian tumour protease (OTU), a MINDY protease, or a ZUFSP protease.

[0007] In some embodiments, the cysteine protease is a USP. In some embodiments, the USP is USP1, USP2, USP3, USP4, USP5, USP6, USP7, USP8, USP9X, USP9Y, USP10, USP11, USP12, USP13, USP14, USP15, USP16, USP17, USP17L2, USP17L3, USP17L4, USP17L5, USP17L7, USP17L8, USP18, USP19, USP20, USP21, USP22, USP23, USP24, USP25, USP26, USP27X, USP28, USP29, USP30, USP31, USP32, USP33, USP34, USP35, USP36, USP37, USP38, USP39, USP40, USP41, USP42, USP43, USP44, USP45, or USP46.

[0008] In some embodiments, the cysteine protease is a UCH. In some embodiments, the UCH is BAP1, UCHL1, UCHL3, or UCHL5.

[0009] In some embodiments, the cysteine protease is a MJD. In some embodiments, the MJD is ATXN3 or ATXN3L.

[0010] In some embodiments, the cysteine protease is a OTU. In some embodiments, the OTU is OTUB1 or OTUB2.

[0011] In some embodiments, the cysteine protease is a MINDY. In some embodiments, the MINDY is MINDY1, MINDY2, MINDY3, or MINDY4.

[0012] In some embodiments, the cysteine protease is a ZUFSP. In some embodiments, the ZUFSP is ZUP1.

[0013] In some embodiments, the deubiquitinase is a metalloprotease. In some embodiments, the metalloprotease is a Jab1/Mov34/Mpr1 Pad1 N-terminal+ (MPN+) (JAMM) domain protease.

[0014] In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 1-112.

[0015] In some embodiments, the catalytic domain comprises a catalytic domain derived from a deubiquitinase at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 1-112.

[0016] In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 113-220 or 293.

[0017] In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 293.

[0018] In some embodiments, the moiety that specifically binds a membrane protein comprises an antibody, or functional fragment or functional variant thereof. In some embodiments, the antibody, or functional fragment or functional variant thereof, comprises a full-length antibody, a single chain variable fragment (scFv), a scFv2, a scFv-Fc, a Fab, a Fab', a F(ab')2, a F(v), a VHH, or a $(VHH)_2$. In some embodiments, the antibody, or functional fragment or functional variant thereof, comprises a VHH or a $(VHH)_2$.

[0019] In some embodiments, the membrane protein is selected from the group consisting of solute carrier family 2, facilitated glucose transporter member 1 (SLC2A1), proline-rich transmembrane protein 2 (PRRT2), usherin (USH2A), protocadherin-19 (PCDH19), tuberin (TSC2), hamartin (TSC1), dystrophin (DMD), Rhodopsin (RHO), protein jagged-1 (JAG1), inositol 1,4,5-trisphosphate receptor type 1 (ITPR1), sugar transporter SWEET1 (SLC50A1), transmembrane protein 258 (TMEM258), or follicle stimulating hormone receptor (FSHR).

[0020] In some embodiments, the membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 221-227 or 243-245.

[0021] In some embodiments, the effector domain is directly operably connected to the targeting domain. In some embodiments, the effector domain is indirectly operably connected to the targeting domain. In some embodiments, the effector domain is indirectly operably connected to the targeting domain via a peptide linker. In some embodiments, the effector domain is indirectly operably connected to the targeting domain via a peptide linker of sufficient length such that the

effector domain and the targeting domain can simultaneous bind the respective target proteins. In some embodiments, the peptide linker comprises the amino acid sequence of any one of SEQ ID NOS: 297-424, or the amino acid sequence of any one of SEQ ID NOS: 297-424 comprising 1, 2, or 3 amino acid modifications. In some embodiments, the peptide linker comprises the amino acid sequence of any one of SEQ ID NOS: 297-306, or the amino acid sequence of any one of SEQ ID NOS: 297-306 comprising 1, 2, or 3 amino acid modifications.

[0022] In some embodiments, the effector domain is operably connected either directly or indirectly to the C terminus of the targeting domain. In some embodiments, the effector moiety is operably connected either directly or indirectly to the N terminus of the targeting domain.

[0023] In one aspect, provided herein are fusion proteins comprising: an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof; and a targeting domain comprising a targeting moiety that specifically binds a membrane protein selected from the group consisting of glutamate receptor ionotropic NMDA 2B (GRIN2B), cystic fibrosis transmembrane conductance regulator (CFTR), sodium channel protein type 1 subunit alpha (SCN1A), copper-transporting ATPase 2 (ATP7B), potassium voltage-gated channel subfamily KQT member 2 (KCNQ2), sodium channel protein type 2 subunit alpha (SCN2A), voltage-dependent P/Q-type calcium channel subunit alpha-1A (CACNA1A), sodium channel protein type 8 subunit alpha (SCN8A), glutamate receptor ionotropic, NMDA 2A (GRIN2A), sodium- and chloride-dependent GABA transporter 1 (SLC6A1), sodium/potassium-transporting ATPase subunit alpha-2 (ATP1A2), sodium/potassium-transporting ATPase subunit alpha-3 (ATP1A3), sodium channel protein type 9 subunit alpha (SCN9A), gamma-aminobutyric acid receptor subunit beta-3 (GABRB3), and potassium voltage-gated channel subfamily KQT member 3 (KCNQ3).

[0024] In some embodiments, the moiety that specifically binds a membrane protein comprises an antibody, or functional fragment or functional variant thereof. In some embodiments, the antibody, or functional fragment or functional variant thereof, comprises a full-length antibody, a single chain variable fragment (scFv), a scFv2, a scFv-Fc, a Fab, a Fab', a F(ab')2, a F(v), a VHH, or a $(VHH)_2$. In some embodiments, the antibody, or functional fragment or functional variant thereof, comprises a VHH or a $(VHH)_2$.

[0025] In some embodiments, the membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino

acid sequence of any one of SEQ ID NOS: 228-245.

[0026] In some embodiments, the deubiquitinase is a cysteine protease or a metalloprotease. In some embodiments, the deubiquitinase is a cysteine protease.

[0027] In some embodiments, the cysteine protease is a ubiquitin-specific protease (USP), a ubiquitin C-terminal hydrolase (UCH), a Machado-Josephin domain protease (MJD), an ovarian tumour protease (OTU), a MINDY protease, or a ZUFSP protease.

[0028] In some embodiments, the cysteine protease is a USP. In some embodiments, the USP is USP1, USP2, USP3, USP4, USP5, USP6, USP7, USP8, USP9X, USP9Y, USP10, USP11, USP12, USP13, USP14, USP15, USP16, USP17, USP17L2, USP17L3, USP17L4, USP17L5, USP17L7, USP17L8, USP18, USP19, USP20, USP21, USP22, USP23, USP24, USP25, USP26, USP27X, USP28, USP29, USP30, USP31, USP32, USP33, USP34, USP35, USP36, USP37, USP38, USP39, USP40, USP41, USP42, USP43, USP44, USP45, or USP46.

[0029] In some embodiments, the cysteine protease is a UCH. In some embodiments, the UCH is BAP1, UCHL1, UCHL3, or UCHL5.

[0030] In some embodiments, the cysteine protease is a MJD. In some embodiments, the MJD is ATXN3 or ATXN3L.

[0031] In some embodiments, the cysteine protease is a OTU. In some embodiments, the OTU is OTUB1 or OTUB2.

[0032] In some embodiments, the cysteine protease is a MINDY. In some embodiments, the MINDY is MINDY1, MINDY2, MINDY3, or MINDY4.

[0033] In some embodiments, the cysteine protease is a ZUFSP. In some embodiments, the ZUFSP is ZUP1.

[0034] In some embodiments, the deubiquitinase is a metalloprotease. In some embodiments, the metalloprotease is a Jab1/Mov34/Mpr1 Pad1 N-terminal+ (MPN+) (JAMM) domain protease.

[0035] In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 1-112.

[0036] In some embodiments, the catalytic domain comprises a catalytic domain derived from a deubiquitinase at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 1-112.

[0037] In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 113-220 or 293.

[0038] In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 293.

[0039] In some embodiments, the effector domain is directly operably connected to the targeting domain. In some embodiments, the effector domain is indirectly operably connected to the targeting domain. In some embodiments, the effector domain is indirectly operably connected to the targeting domain via a peptide linker. In some embodiments, the effector domain is indirectly operably connected to the targeting domain via a peptide linker of sufficient length such that the effector domain and the targeting domain can simultaneous bind the respective target proteins. In some embodiments, the peptide linker comprises the amino acid sequence of any one of SEQ ID NOS: 297-424, or the amino acid sequence of any one of SEQ ID NOS: 297-424 comprising 1, 2, or 3 amino acid modifications. In some embodiments, the peptide linker comprises the amino acid sequence of any one of SEQ ID NOS: 297-306, or the amino acid sequence of any one of SEQ ID NOS: 297-306 comprising 1, 2, or 3 amino acid modifications.

[0040] In some embodiments, the effector domain is operably connected either directly or indirectly to the C terminus of the targeting domain. In some embodiments, the effector moiety is operably connected either directly or indirectly to the N terminus of the targeting domain.

[0041] In one aspect, provided herein are nucleic acid molecules encoding a fusion protein described herein. In some embodiments, the nucleic acid molecule is a DNA molecule. In some embodiments, the nucleic acid molecule is an RNA molecule.

[0042] In one aspect, provided herein are vectors comprising a nucleic acid molecule described herein (e.g., a nucleic acid molecule encoding a fusion protein described herein). In some embodiments, the vector is a plasmid or a viral vector.

[0043] In one aspect, provided herein are viral particles comprising a nucleic acid molecule described herein (e.g., a nucleic acid molecule encoding a fusion protein described herein).

[0044] In one aspect, provided herein are in vitro cell or population of cells comprising a fusion protein described herein, a nucleic acid molecule described herein, or a vector described herein.

[0045] In one aspect, provided herein are pharmaceutical compositions comprising a fusion protein described herein, a nucleic acid described herein, a vector described herein, or a viral particle described herein, and an excipient.

[0046] In one aspect, provided herein are methods of making a fusion protein described herein, comprising introducing into an in vitro cell or population of cells a nucleic acid molecule described herein, a vector described herein, or a viral particle described herein; culturing the cell or population of cells in a culture medium under conditions suitable for expression of the fusion protein, isolating the fusion protein from the culture medium, and optionally purifying the fusion protein.

[0047] In one aspect, provided herein are methods of treating or preventing a disease in a subject comprising administering a fusion protein described herein, a nucleic acid molecule described herein, a vector described herein, a viral particle described herein, or a pharmaceutical composition described herein, to a subject in need thereof. In some embodiments, the subject is human.

[0048] In some embodiments, the disease is associated with decreased expression of a functional version of the mitochondrial protein relative to a non-diseased control. In some embodiments, the disease is associated with decreased stability of a functional version of the mitochondrial protein relative to a non-diseased control. In some embodiments, the disease is associated with increased ubiquitination of the nuclear protein relative to a non-diseased control. In some embodiments, the disease is associated with increased ubiquitination and degradation of the mitochondrial protein relative to a non-diseased control. In some embodiments, the disease is a genetic disease. In some embodiments, the disease is a genetic disease. In some embodiments, the genetic disease is a haploinsufficiency disease.

[0049] In some embodiments, the disease is a GRIN2B-Related Disorder, a SCN2A-Related Disorder, a SCN8A-Related Disorder, SLC6A1-Related Disorder, a PRRT2 Dyskinesia & Epilepsy, a GRIN2A-Related Disorder, a CACNA1A-Related Disorder, a SCN9A Epilepsy, a PCDH19 Encephalopathy, GLUT1 deficiency syndrome, episodic kinesigenic dyskinesia 1, Usher syndrome type 2A, early infantile epileptic encephalopathy type 9, tuberous sclerosis type 2; tuberous sclerosis type 1, a KCNQ2-Related Disorder (e.g., epileptic encephalopathy), Becker Muscular Dystrophy, autosomal Dominant RP, Alagille syndrome 1, Gillespie Syndrome.

[0050] In some embodiments, the disease is early infantile epileptic encephalopathy type 11,

early infantile epileptic encephalopathy type 13, early infantile epileptic encephalopathy type 27, cystic fibrosis, Dravet syndrome, Wilson disease, episodic ataxia type 2; epilepsy (e.g., focal, with speech disorder and with or without mental retardation), myoclonic-atonic epilepsy, alternating hemiplegia of childhood, alternating hemiplegia of childhood type 2, epilepsy type 7, GABRB3 associated epilepsy, or a KCNQ2-Related Disorder (e.g., epileptic encephalopathy).

[0051] In some embodiments, the disease is a GRIN2B-Related Disorder, a SCN2A-Related Disorder, a SCN8A-Related Disorder, SLC6A1-Related Disorder, a PRRT2 Dyskinesia & Epilepsy, a GRIN2A-Related Disorder, a CACNA1A-Related Disorder, a SCN9A Epilepsy, a PCDH19 Encephalopathy, early infantile epileptic encephalopathy type 9, early infantile epileptic encephalopathy type 11, early infantile epileptic encephalopathy type 13, early infantile epileptic encephalopathy type 27, cystic fibrosis, Dravet syndrome, Wilson disease, episodic ataxia type 2; GLUT1 deficiency syndrome, episodic kinesigenic dyskinesia 1, epilepsy (e.g., focal, with speech disorder and with or without mental retardation), KCNQ2 encephalopathy, myoclonic-atonic epilepsy, Usher syndrome type 2A, alternating hemiplegia of childhood, alternating hemiplegia of childhood type 2, epilepsy type 7, GABRB3 associated epilepsy; tuberous sclerosis type 2; tuberous sclerosis type 1, Becker Muscular Dystrophy, autosomal Dominant RP, Alagille syndrome 1, or Gillespie Syndrome.

[0052] In some embodiments, the target membrane protein is GRIN2B, and the disease is a GRIN2B related disorder (e.g., an epileptic encephalopathy); the target membrane protein is GRIN2B, and the disease is an early infantile epileptic encephalopathy; the target membrane protein is GRIN2B, and the disease is early infantile epileptic encephalopathy type 27; the target membrane protein is CFTR, and the disease is cystic fibrosis; the target membrane protein is SCN1A, and the disease is Dravet syndrome; the target membrane protein is ATP7B, and the disease is Wilson disease; the target membrane protein is CACNA1A, and the disease is a CACA1A related disorder; the target membrane protein is CACNA1A, and the disease is episodic ataxia type 2; the target membrane protein is KCNQ2, and the disease is an KCNQ2 encephalopathy; the target membrane protein is KCNQ2, and the disease is an epileptic encephalopathy; the target membrane protein is SCN2A, and the disease is a SCN2A related disorder (e.g., an epileptic encephalopathy); the target membrane protein is SCN2A, and the disease is early infantile epileptic encephalopathy type 11; the target membrane protein is SLC2A1, and the disease is GLUT1 deficiency syndrome; the target membrane protein is SCN8A,

and the disease is a SCN8A related disorder (e.g., an epileptic encephalopathy); the target membrane protein is SCN8A, and the disease is an epileptic encephalopathy; the target membrane protein is SCN8A, and the disease is early infantile epileptic encephalopathy type 13; the target membrane protein is PRRT2, and the disease is a PRRPT2 dyskinesia and/or epilepsy; the target membrane protein is PRRT2, and the disease is an episodic kinesigenic dyskinesia type; the target membrane protein is PRRT2, and the disease is episodic kinesigenic dyskinesia type 1; the target membrane protein is GRIN2A, and the disease is a GRIN2A related disorder; the target membrane protein is GRIN2A, and the disease is epilepsy; the target membrane protein is GRIN2A, and the disease is focal epilepsy; the target membrane protein is GRIN2A, and the disease is focal epilepsy with speech disorder and with or without mental retardation; the target membrane protein is SLC6A1, and the disease is a SLC6A1 related disorder; the target membrane protein is SLC6A1, and the disease is epilepsy; the target membrane protein is SLC6A1, and the disease is myoclonic-atonic epilepsy; the target membrane protein is USH2A, and the disease is Usher syndrome; the target membrane protein is USH2A, and the disease is Usher syndrome type 2A; the target membrane protein is ATP1A2, and the disease is alternating hemiplegia of childhood; the target membrane protein is ATP1A2, and the disease is alternating hemiplegia of childhood type 1; the target membrane protein is ATP1A3, and the disease is alternating hemiplegia of childhood; the target membrane protein is ATP1A3, and the disease is alternating hemiplegia of childhood type 2; the target membrane protein is SCN9A, and the disease an SCN9A epilepsy; the target membrane protein is SCN9A1, and the disease an SCN9A epilepsy; the target membrane protein is SCN9A1, and the disease is epilepsy; the target membrane protein is SCN9A1, and the disease is epilepsy type 7; the target membrane protein is PCDH19, and the disease is PCDH19 encephalopathy; the target membrane protein is PCDH19, and the disease is an early infantile epileptic encephalopathy; the target membrane protein is PCDH19, and the disease is early infantile epileptic encephalopathy type 9; the target membrane protein is GABRB3, and the disease is epilepsy; the target membrane protein is GABRB3, and the disease is GABRB3 associated epilepsy; the target membrane protein is TSC2, and the disease is tuberous sclerosis; the target membrane protein is TSC2, and the disease is tuberous sclerosis type 2; the target membrane protein is TSC2, and the disease is tuberous sclerosis type 1; the target membrane protein is TSC1, and the disease is tuberous sclerosis; the target membrane protein is TSC1, and the disease is tuberous sclerosis type 1; the target membrane protein is TSC1, and the disease is tuberous

sclerosis type 2; the target membrane protein is KCNQ3, and the disease is KCNQ2-Related Disorders (Epileptic Encephalopathy); the target membrane protein is DMD, and the disease is Becker Muscular Dystrophy; the target membrane protein is RHO, and the disease is Autosomal Dominant RP; the target membrane protein is JAG1, and the disease is Alagille syndrome 1; the target membrane protein is ITPR1, and the disease is Gillespie Syndrome; or the target membrane protein is FSHR, and the disease is ovarian dysgenesis 1 (ODG1).

[0053] In some embodiments, the fusion protein is administered at a therapeutically effective dose. In some embodiments, the fusion protein is administered systematically or locally. In some embodiments, the fusion protein is administered intravenously, subcutaneously, or intramuscularly.

[0054] In one aspect, provided herein are fusion proteins described herein, polynucleotides described herein, DNA described herein, RNA described herein, vectors described herein, viral particles described herein, and pharmaceutical compositions described herein for use as a medicament.

[0055] In one aspect, provided herein are fusion proteins described herein, polynucleotides described herein, DNA described herein, RNA described herein, vectors described herein, viral particles described herein, and pharmaceutical compositions described herein for use in treating or inhibiting a genetic disorder.

[0056] In one aspect, provided herein are fusion proteins comprising: (a) an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof; and (b) a targeting domain comprising a targeting moiety that specifically binds a membrane protein that is not an ion channel.

[0057] In some embodiments, the deubiquitinase is a cysteine protease or a metalloprotease.

[0058] In some embodiments, the deubiquitinase is a cysteine protease. In some embodiments, the cysteine protease is a ubiquitin-specific protease (USP), a ubiquitin C-terminal hydrolase (UCH), a Machado-Josephin domain protease (MJD), an ovarian tumour protease (OTU), a MINDY protease, or a ZUFSP protease.

[0059] In some embodiments, the cysteine protease is a USP. In some embodiments, the USP is selected from the group consisting of USP1, USP2, USP3, USP4, USP5, USP6, USP7, USP8, USP9X, USP9Y, USP10, USP11, USP12, USP13, USP14, USP15, USP16, USP17, USP17L2, USP17L3, USP17L4, USP17L5, USP17L7, USP17L8, USP18, USP19, USP20, USP21, USP22,

USP23, USP24, USP25, USP26, USP27X, USP28, USP29, USP30, USP31, USP32, USP33, USP34, USP35, USP36, USP37, USP38, USP39, USP40, USP41, USP42, USP43, USP44, USP45, and USP46.

[0060] In some embodiments, the cysteine protease is a UCH. In some embodiments, the UCH is selected from the group consisting of BAP1, UCHL1, UCHL3, and UCHL5.

[0061] In some embodiments, the cysteine protease is a MJD. In some embodiments, the MJD is selected from the group consisting of ATXN3 and ATXN3L.

[0062] In some embodiments, the cysteine protease is a OTU. In some embodiments, the OTU is selected from the group consisting of OTUB1 and OTUB2.

[0063] In some embodiments, the cysteine protease is a MINDY. In some embodiments, the MINDY is selected from the group consisting of MINDY1, MINDY2, MINDY3, and MINDY4.

[0064] In some embodiments, the cysteine protease is a ZUFSP. In some embodiments, the ZUFSP is ZUP1.

[0065] In some embodiments, the deubiquitinase is a metalloprotease. In some embodiments, the metalloprotease is a Jab1/Mov34/Mpr1 Pad1 N-terminal+ (MPN+) (JAMM) domain protease.

[0066] In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 1-112.

[0067] In some embodiments, the catalytic domain comprises a catalytic domain derived from a deubiquitinase at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 1-112.

[0068] In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 113-220.

[0069] In some embodiments, the moiety that specifically binds a membrane protein comprises an antibody, or functional fragment or functional variant thereof. In some embodiments, the antibody, or functional fragment or functional variant thereof, comprises a full-length antibody, a single chain variable fragment (scFv), a scFv2, a scFv-Fc, a Fab, a Fab', a F(ab')2, a F(v), or a VHH. In some embodiments, the antibody, or functional fragment or functional variant thereof, comprises a VHH.

[0070] In some embodiments, the membrane protein is selected from the group consisting of solute carrier family 2, facilitated glucose transporter member 1 (SLC2A1), proline-rich transmembrane protein 2 (PRRT2), usherin (USH2A), protocadherin-19 (PCDH19), tuberin (TSC2), hamartin (TSC1), and dystrophin (DMD).

[0071] In some embodiments, the membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 221-227 or 243-245.

[0072] In some embodiments, the effector domain is directly fused to the targeting domain.

[0073] In some embodiments, the effector domain is indirectly fused to the targeting domain.

[0074] In some embodiments, the effector domain is indirectly fused to the targeting domain via a peptide linker. In some embodiments, the effector domain is indirectly fused to the targeting domain via a peptide linker of sufficient length such that the effector domain and the targeting domain can simultaneous bind the respective target proteins.

[0075] In some embodiments, the effector domain is fused to the C terminus of the targeting domain. In some embodiments, the effector moiety is fused to the N terminus of the targeting domain.

[0076] In one aspect, provided herein are fusion proteins comprising: (a) an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof; and (b) a targeting domain comprising a targeting moiety that specifically binds a membrane protein selected from the group consisting of glutamate receptor ionotropic NMDA 2B (GRIN2B), cystic fibrosis transmembrane conductance regulator (CFTR), sodium channel protein type 1 subunit alpha (SCN1A), copper-transporting ATPase 2 (ATP7B), potassium voltage-gated channel subfamily KQT member 2 (KCNQ2), sodium channel protein type 2 subunit alpha (SCN2A), voltage-dependent P/Q-type calcium channel subunit alpha-1A (CACNA1A), sodium channel protein type 8 subunit alpha (SCN8A), glutamate receptor ionotropic, NMDA 2A (GRIN2A), sodium- and chloride-dependent GABA transporter 1 (SLC6A1), sodium/potassium-transporting ATPase subunit alpha-2 (ATP1A2), sodium/potassium-transporting ATPase subunit alpha-3 (ATP1A3), sodium channel protein type 9 subunit alpha (SCN9A), gamma-aminobutyric acid receptor subunit beta-3 (GABRB3), and potassium voltage-gated channel subfamily KQT member 3 (KCNQ3).

[0077] In some embodiments, the moiety that specifically binds a membrane protein comprises

an antibody, or functional fragment or functional variant thereof.

[0078] In some embodiments, the antibody, or functional fragment or functional variant thereof, comprises a full-length antibody, a single chain variable fragment (scFv), a scFv2, a scFv-Fc, a Fab, a Fab', a F(ab')2, a F(v), or a VHH. In some embodiments, the antibody, or functional fragment or functional variant thereof, comprises a VHH.

[0079] In some embodiments, the membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 228-245.

[0080] In some embodiments, the deubiquitinase is a cysteine protease or a metalloprotease.

[0081] In some embodiments, the deubiquitinase is a cysteine protease. In some embodiments, the cysteine protease is a ubiquitin-specific protease (USP), a ubiquitin C-terminal hydrolase (UCH), a Machado-Josephin domain protease (MJD), an ovarian tumour protease (OTU), a MINDY protease, or a ZUFSP protease.

[0082] In some embodiments, the cysteine protease is a USP. In some embodiments, the USP is selected from the group consisting of USP1, USP2, USP3, USP4, USP5, USP6, USP7, USP8, USP9X, USP9Y, USP10, USP11, USP12, USP13, USP14, USP15, USP16, USP17, USP17L2, USP17L3, USP17L4, USP17L5, USP17L7, USP17L8, USP18, USP19, USP20, USP21, USP22, USP23, USP24, USP25, USP26, USP27X, USP28, USP29, USP30, USP31, USP32, USP33, USP34, USP35, USP36, USP37, USP38, USP39, USP40, USP41, USP42, USP43, USP44, USP45, and USP46.

[0083] In some embodiments, the cysteine protease is a UCH. In some embodiments, the UCH is selected from the group consisting of BAP1, UCHL1, UCHL3, and UCHL5.

[0084] In some embodiments, the cysteine protease is a MJD. In some embodiments, the MJD is selected from the group consisting of ATXN3 and ATXN3L.

[0085] In some embodiments, the cysteine protease is a OTU. In some embodiments, the OTU is selected from the group consisting of OTUB1 and OTUB2.

[0086] In some embodiments, the cysteine protease is a MINDY. In some embodiments, the MINDY is selected from the group consisting of MINDY1, MINDY2, MINDY3, and MINDY4.

[0087] In some embodiments, the cysteine protease is a ZUFSP. In some embodiments, the ZUFSP is ZUP1.

[0088] In some embodiments, the deubiquitinase is a metalloprotease. In some embodiments,

the metalloprotease is a Jab1/Mov34/Mpr1 Pad1 N-terminal+ (MPN+) (JAMM) domain protease.

[0089] In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 1-112.

[0090] In some embodiments, the catalytic domain comprises a catalytic domain derived from a deubiquitinase at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 1-112.

[0091] In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 113-220.

[0092] In some embodiments, the effector domain is directly fused to the targeting domain.

[0093] In some embodiments, the effector domain is indirectly fused to the targeting domain.

[0094] In some embodiments, the effector domain is indirectly fused to the targeting domain via a peptide linker. In some embodiments, the effector domain is indirectly fused to the targeting domain via a peptide linker of sufficient length such that the effector domain and the targeting domain can simultaneous bind the respective target proteins.

[0095] In some embodiments, the effector domain is fused to the C terminus of the targeting domain. In some embodiments, the effector moiety is fused to the N terminus of the targeting domain.

[0096] In one aspect, provided herein are nucleic acid molecules encoding the fusion protein described herein. In some embodiments, the nucleic acid molecule is a DNA molecule. In some embodiments, the nucleic acid molecule is an RNA molecule.

[0097] In one aspect, provided herein are vectors comprising a nucleic acid molecule described herein. In some embodiments, the vector is a plasmid or a viral vector.

[0098] In one aspect, provided herein are viral particles comprising a nucleic acid described herein.

[0099] In one aspect, described herein is an in vitro cell or population of cells comprising a fusion protein described herein, a nucleic acid molecule described herein, or a vector described herein.

[00100] In one aspect, provided herein are pharmaceutical compositions comprising a fusion

protein described herein, a nucleic acid molecule described herein, a vector described herein, or a viral particle described herein, and an excipient.

[00101] In one aspect, provided herein are methods of making a fusion protein described herein, comprising (a) introducing into an in vitro cell or population of cells a nucleic acid described herein, a vector described herein, or a viral particle described herein; (b) culturing the cell or population of cells in a culture medium under conditions suitable for expression of the fusion protein, (c) isolating the fusion protein from the culture medium, and (d) optionally purifying the fusion protein.

[00102] In one aspect, provided herein are methods of treating a disease in a subject comprising administering a fusion protein described herein, a nucleic acid described herein, a vector described herein, or a viral particle described herein, or a pharmaceutical composition described herein, to a subject in need thereof.

[00103] In some embodiments, the subject is human.

[00104] In some embodiments, the disease is associated with decreased expression of a functional version of the membrane protein relative to a non-diseased control.

[00105] In some embodiments, the disease is associated with decreased stability of a functional version of the membrane protein relative to a non-diseased control.

[00106] In some embodiments, the disease is associated with increased ubiquitination and degradation of the membrane protein relative to a non-diseased control.

[00107] In some embodiments, the disease is a genetic disease.

[00108] In some embodiments, the disease is GLUT1 deficiency syndrome, episodic kinesigenic dyskinesia 1, Usher syndrome type 2A, early infantile epileptic encephalopathy type 9, tuberous sclerosis type 2; tuberous sclerosis type 1, a KCNQ2-Related Disorder (e.g., epileptic encephalopathy), Becker Muscular Dystrophy, autosomal Dominant RP, Alagille syndrome 1, and Gillespie Syndrome.

[00109] In some embodiments, the disease is selected from the group consisting of early infantile epileptic encephalopathy type 11, early infantile epileptic encephalopathy type 13, early infantile epileptic encephalopathy type 27, cystic fibrosis, Dravet syndrome, Wilson disease, episodic ataxia type 2; epilepsy (e.g., focal, with speech disorder and with or without mental retardation), myoclonic-atonic epilepsy, alternating hemiplegia of childhood, alternating hemiplegia of childhood type 2, epilepsy type 7, GABRB3 associated epilepsy, and a KCNQ2-

Related Disorder (e.g., epileptic encephalopathy).

[00110] In some embodiments, the disease is selected from the group consisting of GRIN2B-Related Disorder, early infantile epileptic encephalopathy type 9, early infantile epileptic encephalopathy type 11, early infantile epileptic encephalopathy type 13, early infantile epileptic encephalopathy type 27, cystic fibrosis, Dravet syndrome, Wilson disease, episodic ataxia type 2; GLUT1 deficiency syndrome, episodic kinesigenic dyskinesia 1, epilepsy (e.g., focal, with speech disorder and with or without mental retardation), myoclonic-atonic epilepsy, Usher syndrome type 2A, alternating hemiplegia of childhood, alternating hemiplegia of childhood type 2, epilepsy type 7, GABRB3 associated epilepsy; tuberous sclerosis type 2; tuberous sclerosis type 1, Becker Muscular Dystrophy, autosomal Dominant RP, Alagille syndrome 1, and Gillespie Syndrome.

[00111] In some embodiments, the disease is a haploinsufficiency disease.

[00112] In some embodiments, the fusion protein is administered at a therapeutically effective dose.

[00113] In some embodiments, the fusion protein is administered systematically or locally.

[00114] In some embodiments, the fusion protein is administered intravenously, subcutaneously, or intramuscularly.

[00115] In one aspect, provided herein are nucleic acid molecules encoding the fusion protein described herein. In some embodiments, the nucleic acid molecule is a DNA molecule. In some embodiments, the nucleic acid molecule is an RNA molecule.

[00116] In one aspect, provided herein are vectors comprising a nucleic acid molecule described herein. In some embodiments, the vector is a plasmid or a viral vector.

[00117] In one aspect, provided herein are viral particles comprising a nucleic acid described herein.

[00118] In one aspect, described herein is an in vitro cell or population of cells comprising a fusion protein described herein, a nucleic acid molecule described herein, or a vector described herein.

[00119] In one aspect, provided herein are pharmaceutical compositions comprising a fusion protein described herein, a nucleic acid molecule described herein, a vector described herein, or a viral particle described herein, and an excipient.

[00120] In one aspect, provided herein are methods of making a fusion protein described herein, comprising (a) introducing into an in vitro cell or population of cells a nucleic acid described

herein, a vector described herein, or a viral particle described herein; (b) culturing the cell or population of cells in a culture medium under conditions suitable for expression of the fusion protein, (c) isolating the fusion protein from the culture medium, and (d) optionally purifying the fusion protein.

[00121] In one aspect, provided herein are methods of treating a disease in a subject comprising administering a fusion protein described herein, a nucleic acid described herein, a vector described herein, or a viral particle described herein, or a pharmaceutical composition described herein, to a subject in need thereof.

[00122] In some embodiments, the subject is human.

[00123] In some embodiments, the disease is associated with decreased expression of a functional version of the membrane protein relative to a non-diseased control.

[00124] In some embodiments, the disease is associated with decreased stability of a functional version of the membrane protein relative to a non-diseased control.

[00125] In some embodiments, the disease is associated with increased ubiquitination and degradation of the membrane protein relative to a non-diseased control.

[00126] In some embodiments, the disease is a genetic disease.

[00127] In some embodiments, the disease is early infantile epileptic encephalopathy type 2, Wilson disease, early infantile epileptic encephalopathy type 4, mental retardation autosomal dominant 5, aphasia, alagille syndrome 1, epilepsy, tuberous sclerosis-2, tuberous sclerosis-1, KIF1A-associated neurological disorder, encephalopathy, Phelan-McDermid syndrome, Becker Muscular Dystrophy, RP1, retinitis pigmentosa 1, dilated cardiomyopathy 1G, DYNC1H1 Syndrome, TRIO-Related intellectual disability (ID), and USP9X Development Disorder.

[00128] The method of any one of claims 43-48, wherein the disease is early infantile epileptic encephalopathy type 2, Wilson disease, early infantile epileptic encephalopathy type 4, mental retardation autosomal dominant 5, aphasia primary progressive & FTD (frontotemporal degeneration), alagille syndrome 1, epilepsy familial focal with variable foci 1, tuberous sclerosis-2, tuberous sclerosis-1, KIF1A-associated neurological disorder, encephalopathy, Phelan-McDermid syndrome, Becker Muscular Dystrophy, RP1, retinitis pigmentosa 1, dilated cardiomyopathy 1G, DYNC1H1 Syndrome, TRIO-Related intellectual disability (ID), and USP9X Development Disorder.

[00129] In some embodiments, the disease is a haploinsufficiency disease.

[00130] In some embodiments, the fusion protein is administered at a therapeutically effective dose.

[00131] In some embodiments, the fusion protein is administered systematically or locally.

[00132] In some embodiments, the fusion protein is administered intravenously, subcutaneously, or intramuscularly.

4. BRIEF DESCRIPTION OF THE FIGURES

[00133] **FIGS. 1A-1D** provides a schematic representation of exemplary fusion proteins described herein. **FIG. 1A** is a schematic of an engineered deubiquitinase comprising from N' to C' terminus a VHH that specifically binds a membrane target protein and the catalytic domain of a deubiquitinase. In this specific embodiment, the C-terminus of the VHH is directly connected to the N-terminus of the catalytic domain of the deubiquitinase. **FIG. 1B** is a schematic of an engineered deubiquitinase comprising from N' to C' terminus the catalytic domain of a deubiquitinase that specifically binds a membrane target protein and a VHH that specifically binds a membrane target protein. In this specific embodiment, the C-terminus of the catalytic domain of the deubiquitinase is directly connected to the N-terminus of the VHH. **FIG. 1C** is a schematic of an engineered deubiquitinase comprising from N' to C' terminus a VHH that specifically binds a membrane target protein and the catalytic domain of a deubiquitinase. In this specific embodiment, the C-terminus of the VHH is indirectly connected to the N-terminus of the catalytic domain of the deubiquitinase through a peptide linker. **FIG. 1D** is a schematic of an engineered deubiquitinase comprising from N' to C' terminus the catalytic domain of a deubiquitinase that specifically binds a membrane target protein and a VHH that specifically binds a membrane target protein. In this specific embodiment, the C-terminus of the catalytic domain of the deubiquitinase is indirectly connected to the N-terminus of the VHH through a peptide linker.

[00134] **FIG. 2** is a schematic representation of the assay utilized in Example 3, to screen the effect of targeted deubiquitination of different membrane proteins on target protein expression.

[00135] **FIG. 3** is a bar graph depicting the fold change in KCNQ1 protein expression relative to control (as indicated).

[00136] **FIG. 4** is a bar graph depicting the fold change in SCN1A protein expression relative to control (as indicated).

[00137] **FIG. 5** is a bar graph depicting the fold change in GRIN2B protein expression relative

to control (as indicated).

[00138] **FIG. 6** is a bar graph depicting the fold change in SLC50A1 protein expression relative to control (deubiquitinase without the nanobody targeting the alfa-tag).

[00139] **FIG. 7** is a bar graph depicting the fold change in TREM258 protein expression relative to control (deubiquitinase without the nanobody targeting the alfa-tag).

[00140] **FIG. 8** is a bar graph depicting the fold change in FSHR protein expression relative to control (deubiquitinase without the nanobody targeting the alfa-tag).

5. DETAILED DESCRIPTION

5.1 Overview

[00141] Ubiquitination is the process by which ubiquitin ligases mediate the addition of ubiquitin, a 76 amino acid regulatory protein, to a substrate protein. Ubiquitination generally starts by the attachment of a single ubiquitin molecule to a lysine amino acid residue of the substrate protein. Mevissen T. et al. Mechanisms of Deubiquitinase Specificity and Regulation Annual Review of Biochemistry 86:1, 159-192 (2017), the entire contents of which is incorporated by reference herein. These monoubiquitination events are abundant and serve various functions. Ubiquitin itself contains seven lysine residues, all of which can be ubiquitinated resulting in polyubiquitinated proteins. Komander, D. et al. Breaking the chains: structure and function of the deubiquitinases. Nat Rev Mol Cell Biol 10, 550–563 (2009), the entire contents of which is incorporated by reference herein. Mono and polyubiquitination can have multiple effects on the substrate protein, including marking the substrate protein for degradation via the proteasome, altering the protein's cellular location, altering the protein's activity, and/or promoting or preventing normal protein interactions. See e.g., Hershko A. et al. The ubiquitin system. Annu Rev Biochem. 67:425-79 (1998); Nandi D, et al. The ubiquitin-proteasome system. J Biosci. Mar;31(1):137-55 (2006), the entire contents of each of which is incorporated by reference herein. The effects of ubiquitination can be reversed or prevented by removing the ubiquitin protein(s) from the substrate protein. The removal of ubiquitin from a substrate protein is mediated by deubiquitinase (DUB) proteins. *Id.*

[00142] Numerous genetic diseases are associated with or caused by a decrease in the level of expression of a functional membrane protein or the stability of the membrane protein. For example, haploinsufficiency genetic diseases are caused by the presence a single copy of a wild-type allele

in heterozygous combination with a loss of function variant allele, wherein the level of functional protein expressed is insufficient to produce the standard phenotype. See e.g., Johnson, A. et al, Causes and effects of haploinsufficiency. Biol Rev, 94: 1774-1785 (2019), the entire contents of which is incorporated by reference herein. Haploinsufficiency can arise from a de novo or inherited loss-of-function mutation in the variant allele, such that it produces little or no functional protein. Other genetic disorders result from the ubiquitination and subsequent degradation of variant but functional proteins, resulting in a decrease in expression of the functional protein.

[00143] The present disclosure provides, *inter alia*, novel fusion proteins that comprise the catalytic domain (or functional fragment thereof) of a deubiquitinase and a targeting moiety, such as a VHH, that specifically binds to a target membrane protein. In some embodiments, decreased expression of a functional version of the target membrane protein or decreased stability of a functional version of the target membrane protein is associated with a disease phenotype. As such, the fusion proteins described herein are particularly useful in the treatment of genetic diseases characterized by a decrease in the level of expression of a functional target membrane protein or the stability of the target membrane protein. Upon expression of the fusion protein by host cells, the catalytic domain of the deubiquitinase will be specifically targeted to the target membrane protein and deubiquitinated, resulting in increased expression of the target membrane protein, e.g., to a level sufficient to alleviate the disease phenotype.

5.2 Definitions

[00144] The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described.

[00145] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure is related. For example, the Concise Dictionary of Biomedicine and Molecular Biology, Juo, Pei-Show, 2nd ed., 2002, CRC Press; The Dictionary of Cell and Molecular Biology, 3rd ed., 1999, Academic Press; and the Oxford Dictionary Of Biochemistry And Molecular Biology, Revised, 2000, Oxford University Press, provide one of skill with a general dictionary of many of the terms used in this disclosure.

[00146] It is to be understood that the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of any subject matter

claimed. In this application, the use of the singular includes the plural unless specifically stated otherwise.

[00147] It must be noted that, as used in the specification and the appended claims, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Furthermore, use of the term "including" as well as other forms, such as "include," "includes," and "included," is not limiting.

[00148] It is understood that wherever aspects are described herein with the language "comprising," otherwise analogous aspects described in terms of "consisting of" and/or "consisting essentially of" are also provided.

[00149] The term "and/or" where used herein is to be taken as specific disclosure of each of the two specified features or components with or without the other. Thus, the term "and/or" as used in a phrase such as "A and/or B" herein is intended to include "A and B," "A or B," "A" (alone), and "B" (alone). Likewise, the term "and/or" as used in a phrase such as "A, B, and/or C" is intended to encompass each of the following aspects: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).

[00150] Units, prefixes, and symbols are denoted in their Système International de Unites (SI) accepted form. Numeric ranges are inclusive of the numbers defining the range. The headings provided herein are not limitations of the various aspects of the disclosure, which can be had by reference to the specification as a whole. Accordingly, the terms defined immediately below are more fully defined by reference to the specification in its entirety.

[00151] As described herein, any concentration range, percentage range, ratio range or integer range is to be understood to include the value of any integer within the recited range and, when appropriate, fractions thereof (such as one tenth and one hundredth of an integer), unless otherwise indicated.

[00152] The terms "about" or "comprising essentially of" refer to a value or composition that is within an acceptable error range for the particular value or composition as determined by one of ordinary skill in the art, which will depend in part on how the value or composition is measured or determined, i.e., the limitations of the measurement system. For example, "about" or "comprising essentially of" can mean within 1 or more than 1 standard deviation per the practice in the art. Alternatively, "about" or "comprising essentially of" can mean a range of up to 20%. Furthermore, particularly with respect to biological systems or processes, the terms can mean up to an order of

magnitude or up to 5-fold of a value. When particular values or compositions are provided in the application and claims, unless otherwise stated, the meaning of "about" or "comprising essentially of" should be assumed to be within an acceptable error range for that particular value or composition.

[00153] As used herein, the term "catalytic domain" in reference to a deubiquitinase refers to an amino acid sequence, or a variant thereof, of a deubiquitinase that is capable of mediating deubiquitination of a target protein. The catalytic domain may comprise a naturally occurring amino acid sequence of a deubiquitinase or it may comprise a variant amino acid sequence of a naturally occurring deubiquitinase. The catalytic domain may comprise the minimum amino acid sequence of a deubiquitinase to mediate deubiquitination of a target protein. The catalytic domain may comprise more than the minimum amino acid sequence of a deubiquitinase to mediate deubiquitination of a target protein.

[00154] The terms "polynucleotide" and "nucleic acid sequence" are used interchangeably herein and refer to a polymer of DNA or RNA. The polynucleotide sequence can be single-stranded or double-stranded; contain natural, non-natural, or altered nucleotides; and contain a natural, non-natural, or altered internucleotide linkage, such as a phosphoroamidate linkage or a phosphorothioate linkage, instead of the phosphodiester found between the nucleotides of an unmodified polynucleotide sequence. Polynucleotide sequences include, but are not limited to, all polynucleotide sequences which are obtained by any means available in the art, including, without limitation, recombinant means, *e.g.,* the cloning of polynucleotide sequences from a recombinant library or a cell genome, using ordinary cloning technology and polymerase chain reaction, and the like, and by synthetic means.

[00155] The terms "amino acid sequence" and "polypeptide" are used interchangeably herein and refer to a polymer of amino acids connected by one or more peptide bonds.

[00156] The term "functional variant" as used herein in reference to a protein or polypeptide refers to a protein that comprises at least one amino acid modification (*e.g.,* a substitution, deletion, addition) compared to the amino acid sequence of a reference protein, that retains at least one particular function. In some embodiments, the reference protein is a wild type protein. For example, a functional variant of an IL-2 protein can refer to an IL-2 protein comprising an amino acid substitution as compared to a wild type IL-2 protein that retains the ability to bind the intermediate affinity IL-2 receptor but abrogates the ability of the protein to bind the high affinity

IL-2 receptor. Not all functions of the reference wild type protein need be retained by the functional variant of the protein. In some instances, one or more functions are selectively reduced or eliminated.

[00157] The term "functional fragment" as used herein in reference to a protein or polypeptide refers to a fragment of a reference protein that retains at least one particular function. For example, a functional fragment of an anti-HER2 antibody can refer to a fragment of the anti-HER2 antibody that retains the ability to specifically bind the HER2 antigen. Not all functions of the reference protein need be retained by a functional fragment of the protein. In some instances, one or more functions are selectively reduced or eliminated.

[00158] As used herein, the term "modification," with reference to a polynucleotide sequence, refers to a polynucleotide sequence that comprises at least one substitution, alteration, inversion, addition, or deletion of nucleotide compared to a reference polynucleotide sequence. Modifications can include non-naturally nucleotides. As used herein, the term "modification," with reference to an amino acid sequence refers to an amino acid sequence that comprises at least one substitution, alteration, inversion, addition, or deletion of an amino acid residue compared to a reference amino acid sequence. Modifications can include the inclusion of non-naturally occurring amino acid residues.

[00159] As used herein, the term "derived from" with reference to an amino acid sequence refers to an amino acid sequence that has at least 80% sequence identity to a reference naturally occurring amino acid sequence. For example, a catalytic domain derived from a naturally occurring deubiquitinase means that the catalytic domain has an amino acid sequence with at least 80% sequence identity to the sequence of the deubiquitinase catalytic domain from which it is derived. The term "derived from" as used herein does not denote any specific process or method for obtaining the amino acid sequence. For example, the amino acid sequence can be chemically or recombinantly synthesized.

[00160] The term "fusion protein" and grammatical equivalents as used herein refers to a protein that comprises an amino acid sequence derived from at least two separate proteins. The amino acid sequence of the at least two separate proteins can be directly connected through a peptide bond; or can be operably connected through an amino acid linker. Therefore, the term fusion protein encompasses embodiments, wherein the amino acid sequence of e.g., Protein A is directly connected to the amino acid sequence of Protein B through a peptide bond (Protein A –

Protein B), and embodiments, wherein the amino acid sequence of e.g., Protein A is operably connected to the amino acid sequence of Protein B through an amino acid linker (Protein A – linker – Protein B).

[00161] The term "fuse" and grammatical equivalents thereof as used herein refers to the operable connection of an amino acid sequence derived from one protein to the amino acid sequence derived from different protein. The term fuse encompasses both a direct connection of the two amino acid sequences through a peptide bond, and the indirect connection through an amino acid linker.

[00162] An "isolated antibody" refers to an antibody that is substantially free of other antibodies having different antigenic specificities (e.g., an isolated antibody that binds specifically to HER2 is substantially free of antibodies that bind specifically to antigens other than HER2). An isolated antibody that binds specifically to HER2 may, however, cross-react with other antigens, such as HER2 molecules from different species. Moreover, an isolated antibody may be substantially free of other cellular material and/or chemicals. By comparison, an "isolated" nucleic acid refers to a nucleic acid composition of matter that is markedly different, i.e., has a distinctive chemical identity, nature and utility, from nucleic acids as they exist in nature. For example, an isolated DNA, unlike native DNA, is a freestanding portion of a native DNA and not an integral part of a larger structural complex, the chromosome, found in nature. Further, an isolated DNA, unlike native DNA, can be used as a PCR primer or a hybridization probe for, among other things, measuring gene expression and detecting biomarker genes or mutations for diagnosing disease or predicting the efficacy of a therapeutic. An isolated nucleic acid may also be purified so as to be substantially free of other cellular components or other contaminants, e.g., other cellular nucleic acids or proteins, using standard techniques well known in the art.

[00163] As used herein, the term "antibody" or "antibodies" are used in the broadest sense and encompasses various antibody structures, including but not limited to monoclonal antibodies, polyclonal antibodies, multispecific antibodies (e.g., bispecific antibodies), and antibody fragments so long as they exhibit the desired antigen-binding activity (i.e. antigen binding fragments as defined herein). The term antibody thus includes, for example, include full-length antibodies, antigen-binding fragments of full-length antibodies, molecules comprising antibody CDRs, VH regions, and/or VL regions; and antibody-like scaffolds (e.g., fibronectins). Examples of antibodies include, without limitation, monoclonal antibodies, recombinantly produced

antibodies, monospecific antibodies, multispecific antibodies (including bispecific antibodies), human antibodies, humanized antibodies, chimeric antibodies, immunoglobulins, synthetic antibodies, tetrameric antibodies comprising two heavy chain and two light chain molecules, an antibody light chain monomer, an antibody heavy chain monomer, an antibody light chain dimer, an antibody heavy chain dimer, an antibody light chain- antibody heavy chain pair, intrabodies, heteroconjugate antibodies, antibody-drug conjugates, single domain antibodies (e.g.,VHH, $(VHH)_2$), monovalent antibodies, single chain antibodies, single-chain Fvs (scFv; $(scFv)_2$), camelized antibodies, affybodies, Fab fragments (e.g., Fab, single chain Fab (scFab), $F(ab')_2$ fragments, disulfide-linked Fvs (sdFv), anti-idiotypic (anti-Id) antibodies (including, *e.g.*, anti-anti-Id antibodies), diabodies, tribodies, and antibody-like scaffolds (e.g., fibronectins), Fc fusions (e.g., Fab-Fc, scFv-Fc, VHH-Fc, $(scFv)_2$-Fc, $(VHH)_2$-Fc, and antigen-binding fragments of any of the above, and conjugates or fusion proteins comprising any of the above. In certain embodiments, antibodies described herein refer to polyclonal antibody populations. In certain embodiments, antibodies described herein refer to monoclonal antibody populations. Antibodies can be of any type (*e.g.*, IgG, IgE, IgM, IgD, IgA or IgY), any class (*e.g.*, IgG_1, IgG_2, IgG_3, IgG_4, IgA_1 or IgA_2), or any subclass (*e.g.*, IgG_{2a} or IgG_{2b}) of immunoglobulin (Ig) molecule. In certain embodiments, antibodies described herein are IgG antibodies, or a class (*e.g.*, human IgG_1 or IgG_4) or subclass thereof. In a specific embodiment, the antibody is a humanized monoclonal antibody. In another specific embodiment, the antibody is a human monoclonal antibody.

[00164] The term "full-length antibody," as used herein refers to an antibody having a structure substantially similar to a native antibody structure comprising two heavy chains and two light chains interconnected by disulfide bonds. In some embodiments, the two heavy chains comprise a substantially identical amino acid sequence; and the two light chains comprise a substantially identical amino acid sequence. Antibody chains may be substantially identical but not entirely identical if they differ due to post-translational modifications, such as C-terminal cleavage of lysine residues, alternative glycosylation patterns, etc.

[00165] The terms "antigen binding fragment" and "antigen binding domain" are used interchangeably herein and refer to one or more polypeptides, other than a full-length antibody, that is capable of specifically binding to antigen and comprises a portion of a full-length antibody (e.g., a VH, a VL). Exemplary antigen binding fragments include, but are not limited to, single domain antibodies (e.g.,VHH, $(VHH)_2$), single chain antibodies, single-chain Fvs (scFv; $(scFv)_2$),

camelized antibodies, affybodies, Fab fragments (e.g., Fab, single chain Fab (scFab), $F(ab')_2$ fragments, and disulfide-linked Fvs (sdFv). The antigen binding domain can be part of a larger protein, e.g., a full-length antibody.

[00166] The term "$(scFv)_2$" as used herein refers to an antibody that comprises a first and a second scFv operably connected (e.g., via a linker). The first and second scFv can specifically bind the same or different antigens. In some embodiments, the first and second scFv are operably connected by an amino via an amino acid linker.

[00167] The term "$(VHH)_2$" as used herein refers to an antibody that comprises a first and a second VHH operably connected (e.g., via a linker). The first and the second VHH can specifically bind the same or different antigens. In some embodiments, the first and second VHH are operably connected by an amino via an amino acid linker.

[00168] The term "Fab-Fc" as used herein refers to an antibody that comprises a Fab operably linked to an Fc domain or a subunit of an Fc domain. A full-length antibody described herein comprises two Fabs, one Fab operably connected to one Fc domain and the other Fab operably connected to a second Fc domain.

[00169] The term "scFv-Fc" as used herein refers to an antibody that comprises a scFv operably linked to an Fc domain or subunit of an Fc domain.

[00170] The term "VHH-Fc" as used herein refers to an antibody that comprises a VHH operably linked to an Fc domain or a subunit of an Fc domain.

[00171] The term "$(scFv)_2$-Fc" as used herein refers to a $(scFv)_2$ operably linked to an Fc domain or a subunit of an Fc domain.

[00172] The term "$(VHH)_2$-Fc" as used herein refers to $(VHH)_2$ operably linked to an Fc domain or a subunit of an Fc domain.

[00173] "Antibody-like scaffolds" are known in the art, for example, fibronectin and designed ankyrin repeat proteins (DARPins) have been used as alternative scaffolds for antigen-binding domains, *see, e.g.,* Gebauer and Skerra, Engineered protein scaffolds as next-generation antibody therapeutics. Curr Opin Chem Biol 13:245-255 (2009) and Stumpp et al., Darpins: A new generation of protein therapeutics. Drug Discovery Today 13: 695-701 (2008). Exemplary antibody-like scaffold proteins include, but are not limited to, lipocalins (Anticalin), Protein A-derived molecules such as Z-domains of Protein A (Affibody), an A-domain (Avimer/Maxibody), a serum transferrin (trans-body); a designed ankyrin repeat protein (DARPin), VNAR fragments,

a fibronectin (AdNectin), a C-type lectin domain (Tetranectin); a variable domain of a new antigen receptor beta-lactamase (VNAR fragments), a human gamma-crystallin or ubiquitin (Affilin molecules); a kunitz type domain of human protease inhibitors, microbodies such as the proteins from the knottin family, peptide aptamers and fibronectin (adnectin).

[00174] As used herein, the term "CDR" or "complementarity determining region" means the noncontiguous antigen combining sites found within the variable region of both heavy and light chain polypeptides. These particular regions have been described by Kabat *et al.*, J. Biol. Chem. 252, 6609-6616 (1977) and Kabat *et al.*, Sequences of protein of immunological interest. (1991), all of which are herein incorporated by reference in their entireties. Unless otherwise specified, the term "CDR" is a CDR as defined by Kabat *et al.*, J. Biol. Chem. 252, 6609-6616 (1977) and Kabat *et al.*, Sequences of protein of immunological interest. (1991).

[00175] As used herein, the term "framework (FR) amino acid residues" refers to those amino acids in the framework region of an antibody variable region. The term "framework region" or "FR region" as used herein, includes the amino acid residues that are part of the variable region, but are not part of the CDRs (*e.g.*, using the Kabat definition of CDRs).

[00176] As used herein, the term "heavy chain" when used in reference to an antibody can refer to any distinct type, *e.g.*, alpha (α), delta (δ), epsilon (ε), gamma (γ), and mu (μ), based on the amino acid sequence of the constant domain, which give rise to IgA, IgD, IgE, IgG, and IgM classes of antibodies, respectively, including subclasses of IgG, *e.g.*, IgG_1, IgG_2, IgG_3, and IgG_4.

[00177] As used herein, the term "light chain" when used in reference to an antibody can refer to any distinct type, *e.g.*, kappa (κ) or lambda (λ) based on the amino acid sequence of the constant domains. Light chain amino acid sequences are well known in the art. In specific embodiments, the light chain is a human light chain.

[00178] As used herein, the terms "variable region" refers to a portion of an antibody, generally, a portion of a light or heavy chain, typically about the amino-terminal 110 to 120 amino acids or 110 to 125 amino acids in the mature heavy chain and about 90 to 115 amino acids in the mature light chain, which differ extensively in sequence among antibodies and are used in the binding and specificity of a particular antibody for its particular antigen. The variability in sequence is concentrated in those regions called complementarity determining regions (CDRs) while the more highly conserved regions in the variable domain are called framework regions (FR). Without wishing to be bound by any particular mechanism or theory, it is believed that the CDRs of the

light and heavy chains are primarily responsible for the interaction and specificity of the antibody with antigen. In certain embodiments, the variable region is a human variable region. In certain embodiments, the variable region comprises rodent or murine CDRs and human framework regions (FRs). In particular embodiments, the variable region is a primate (*e.g.*, non-human primate) variable region. In certain embodiments, the variable region comprises rodent or murine CDRs and primate (*e.g.*, non-human primate) framework regions (FRs).

[00179] The terms "VL" and "VL domain" are used interchangeably to refer to the light chain variable region of an antibody.

[00180] The terms "VH" and "VH domain" are used interchangeably to refer to the heavy chain variable region of an antibody.

[00181] As used herein, the terms "constant region" and "constant domain" are interchangeable and are common in the art. The constant region is an antibody portion, *e.g.*, a carboxyl terminal portion of a light and/or heavy chain which is not directly involved in binding of an antibody to antigen but which can exhibit various effector functions, such as interaction with an Fc receptor (*e.g.*, Fc gamma receptor). The constant region of an immunoglobulin (Ig) molecule generally has a more conserved amino acid sequence relative to an immunoglobulin (Ig) variable domain.

[00182] The term "Fc region" as used herein refers to the C-terminal region of an immunoglobulin (Ig) heavy chain that comprises from N- to C-terminus at least a CH2 domain operably connected to a CH3 domain. In some embodiments, the Fc region comprises an immunoglobulin (Ig) hinge region operably connected to the N-terminus of the CH2 domain. Examples of proteins with engineered Fc regions can be found in Saunders 2019 (K. O. Saunders, "*Conceptual Approaches to Modulating Antibody Effector Functions and Circulation Half-Life*," 2019, Frontiers in Immunology, V. 10, Art. 1296, pp. 1-20, which is incorporated by reference herein).

[00183] As used herein, the term "EU numbering system" refers to the EU numbering convention for the constant regions of an antibody, as described in Edelman, G.M. *et al.*, Proc. Natl. Acad. USA, 63, 78-85 (1969) and Kabat *et al*, Sequences of Proteins of Immunological Interest, U.S. Dept. Health and Human Services, 5th edition, 1991, each of which is herein incorporated by reference in its entirety.

[00184] As used herein, the term "Kabat numbering system" refers to the Kabat numbering convention for variable regions of an antibody, see e.g., Kabat *et al*, Sequences of Proteins of

Immunological Interest, U.S. Dept. Health and Human Services, 5th edition, 1991. Unless otherwise noted, numbering of the variable regions of an antibody are denoted according to the Kabat numbering system.

[00185] As used herein, the terms "specifically binds," refers to molecules that bind to an antigen (*e.g.*, epitope or immune complex) as such binding is understood by one skilled in the art. For example, a molecule that specifically binds to an antigen can bind to other peptides or polypeptides, generally with lower affinity as determined by, *e.g.*, immunoassays, BIAcore®, KinExA 3000 instrument (Sapidyne Instruments, Boise, ID), or other assays known in the art. In a specific embodiment, molecules that specifically bind to an antigen bind to the antigen with a K_A that is at least 2 logs (*e.g.*, factors of 10), 2.5 logs, 3 logs, 4 logs or greater than the K_A when the molecules bind non-specifically to another antigen. The skilled worker will appreciate that an antibody, as described herein, can specifically bind to more than one antigen (*e.g.*, via different regions of the antibody molecule). The term specifically binds includes molecules that are cross reactive with the same antigen of a different species. For example, an antigen binding domain that specifically binds human CD20 may be cross reactive with CD20 of another species (e.g., cynomolgus monkey, or murine), and still be considered herein to specifically bind human CD20.

[00186] "Affinity" refers to the strength of the sum total of non-covalent interactions between a single binding site of a molecule (e.g., a receptor) and its binding partner (e.g., a ligand). Unless indicated otherwise, as used herein, "binding affinity" refers to intrinsic binding affinity, which reflects a 1 : 1 interaction between members of a binding pair (e.g., an antigen binding moiety and an antigen, or a receptor and its ligand). The affinity of a molecule X for its partner Y can generally be represented by the dissociation constant (KD), which is the ratio of dissociation and association rate constants (koff and kon, respectively). Thus, equivalent affinities may comprise different rate constants, as long as the ratio of the rate constants remains the same. Affinity can be measured by well-established methods known in the art, including those described herein. A particular method for measuring affinity is Surface Plasmon Resonance (SPR).

[00187] The determination of "percent identity" between two sequences (e.g., amino acid sequences or nucleic acid sequences) can be accomplished using a mathematical algorithm. Identity measures the percent of identical matches between the smaller of two or more sequences with gap alignments (if any) addressed by a particular mathematical model or computer program (i.e., "algorithms"). A specific, non-limiting example of a mathematical algorithm utilized for the

comparison of two sequences is the algorithm of Karlin S & Altschul SF (1990) PNAS 87: 2264-2268, modified as in Karlin S & Altschul SF (1993) PNAS 90: 5873-5877, each of which is herein incorporated by reference in its entirety. Such an algorithm is incorporated into the BLASTN, BLASTP, BLASTX programs of Altschul SF et al., (1990) J Mol Biol 215: 403, which is herein incorporated by reference in its entirety. BLAST nucleotide searches can be performed with the NBLAST nucleotide program parameters set, e.g., for score=100, wordlength=12 to obtain nucleotide sequences homologous to a nucleic acid molecule described herein. BLAST protein searches can be performed with the BLASTP program parameters set, e.g., default settings; to obtain amino acid sequences homologous to a protein molecule described herein. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul SF et al., (1997) Nuc Acids Res 25: 3389-3402, which is herein incorporated by reference in its entirety. Alternatively, PSI BLAST can be used to perform an iterated search which detects distant relationships between molecules (Id.). When utilizing BLAST, Gapped BLAST, and PSI Blast programs, the default parameters of the respective programs (e.g., of BLASTP and BLASTN) can be used (see, e.g., National Center for Biotechnology Information (NCBI) on the worldwide web, ncbi.nlm.nih.gov). Another specific, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, 1988, CABIOS 4:11-17, which is herein incorporated by reference in its entirety. Such an algorithm is incorporated in the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used. The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating percent identity, typically only exact matches are counted. As described above, the percent identity is based on the amino acid matches between the smaller of two proteins. Therefore, for example, using NCBI Basic Local Alignment Tool - BLASTP program on the default settings (Search Parameters: word size 3, expect value 0.05, hitlist 100, Gapcosts 11,1; Matrix BLOSUM62, Filter string: F; Genetic Code: 1; Window Size: 40; Threshold: 11; Composition Based Stats: 2; Karlin-Altschul Statistics: Lambda: 0.31293; 0.267; K: 0.132922; 0.041; H: 0.401809; 0.14; and Relative Statistics: Effective search space: 288906); the percent identity between SEQ ID NO: 80 and SEQ ID NO: 293 is 100% identity.

[00188] As used herein, the term “operably connected” refers to a linkage of polynucleotide

sequence elements or amino acid sequence elements in a functional relationship. For example, a polynucleotide sequence is operably connected when it is placed into a functional relationship with another polynucleotide sequence. In some embodiments, a transcription regulatory polynucleotide sequence *e.g.,* a promoter, enhancer, or other expression control element is operably-linked to a polynucleotide sequence that encodes a protein if it affects the transcription of the polynucleotide sequence that encodes the protein.

[00189] The terms "subject" and "patient" are used interchangeably herein and include any human or nonhuman animal. The term "nonhuman animal" includes, but is not limited to, vertebrates such as nonhuman primates, sheep, dogs, and rodents such as mice, rats and guinea pigs. In some embodiments, the subject is a human.

[00190] As used herein, the term "administering" refers to the physical introduction of a therapeutic agent (or a precursor of the therapeutic agent that is metabolized or altered within the body of the subject to produce the therapeutic agent in vivo) to a subject, using any of the various methods and delivery systems known to those skilled in the art. Exemplary routes of include intravenous, intramuscular, subcutaneous, intraperitoneal, spinal or other parenteral routes of administration, for example by injection or infusion. The term "parenteral administration" as used herein means modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intralymphatic, intralesional, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal, epidural and intrasternal injection and infusion, as well as *in vivo* electroporation. A therapeutic agent may be administered via a non-parenteral route, or orally. Other non-parenteral routes include a topical, epidermal or mucosal route of administration, for example, intranasally, vaginally, rectally, sublingually or topically. Administering can also be performed, for example, once, a plurality of times, and/or over one or more extended periods.

[00191] A "therapeutically effective amount" or "therapeutically effective dose" of a drug or therapeutic agent is any amount of the drug that, when used alone or in combination with another therapeutic agent, protects a subject against the onset of a disease or promotes disease regression evidenced by a decrease in severity of disease symptoms, an increase in frequency and duration of disease symptom-free periods, or a prevention of impairment or disability due to the disease affliction. The ability of a therapeutic agent to promote disease regression can be evaluated using

a variety of methods known to the skilled practitioner, such as in human subjects during clinical trials, in animal model systems predictive of efficacy in humans, or by assaying the activity of the agent in in vitro assays.

[00192] The terms "disease," "disorder," and "syndrome" are used interchangeably herein.

[00193] As used herein, the terms "treat," treating," "treatment," and the like refer to reducing or ameliorating a disease and/or symptom(s) associated therewith or obtaining a desired pharmacologic and/or physiologic effect. It will be appreciated that, although not precluded, treating a disease does not require that the disease or symptoms associated therewith be completely eliminated. In some embodiments, the effect is therapeutic, i.e., without limitation, the effect partially or completely reduces, diminishes, abrogates, abates, alleviates, decreases the intensity of, or cures a disease and/or adverse symptom attributable to the disease. In some embodiments, the effect is preventative, i.e., the effect protects or prevents an occurrence or reoccurrence of a disease. To this end, the presently disclosed methods comprise administering a therapeutically effective amount of a compositions as described herein.

5.3 Fusion Proteins

[00194] In certain aspects, provided herein are fusion proteins that comprise an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof; and a targeting domain comprising a moiety that specifically binds a target cytosolic protein.

5.3.1 Effector Domain

[00195] In some embodiments, the effector domain comprises a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof. In some embodiments, the deubiquitinase is human. In some embodiments, the catalytic domain is derived from a naturally occurring deubiquitinase (e.g., a naturally occurring human deubiquitinase).

[00196] In some embodiments, the amino acid sequence of the effector domain comprises the amino acid sequence of a full length deubiquitinase. In some embodiments, the amino acid sequence of the effector domain comprises the amino acid sequence of a catalytic domain of a deubiquitinase and an additional amino acid sequence at the N-terminal, C-terminal, or N-terminal and C-terminal end of the catalytic domain.

[00197] In some embodiments, the catalytic domain comprises a naturally occurring amino acid sequence of a deubiquitinase. In some embodiments, the catalytic domain comprises a variant of a naturally occurring deubiquitinase. In some embodiments, the amino acid sequence of the catalytic domain of the fusion protein is at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of a naturally occurring deubiquitinase. In some embodiments, the amino acid sequence of the catalytic domain of the fusion protein comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, or 20 amino acid modifications compared to the amino acid sequence of the catalytic domain of a naturally occurring deubiquitinase.

[00198] In some embodiments, the catalytic domain comprises the minimum amino acid sequence of a naturally occurring deubiquitinase sufficient to mediate deubiquitination of a target protein. In some embodiments, the catalytic domain comprises more than the minimum amino acid sequence of a naturally occurring deubiquitinase sufficient to mediate deubiquitination of a target protein.

[00199] In some embodiments, the deubiquitinase is a cysteine protease or a metalloprotease. In some embodiments, the deubiquitinase is a cysteine protease. In some embodiments, the deubiquitinase is a metalloprotease. In some embodiments, the deubiquitinase is a ubiquitin-specific protease (USP), a ubiquitin C-terminal hydrolase (UCH), a Machado-Josephin domain protease (MJD), an ovarian tumor protease (OTU), a MINDY protease, or a ZUFSP protease.

[00200] Exemplary deubiquitinases include, but are not limited to, USP1, USP2, USP3, USP4, USP5, USP6, USP7, USP8, USP9X, USP9Y, USP10, USP11, USP12, USP13, USP14, USP15, USP16, USP17, USP17L2, USP17L3, USP17L4, USP17L5, USP17L7, USP17L8, USP18, USP19, USP20, USP21, USP22, USP23, USP24, USP25, USP26, USP27X, USP28, USP29, USP30, USP31, USP32, USP33, USP34, USP35, USP36, USP37, USP38, USP39, USP40, USP41, USP42, USP43, USP44, USP45, USP46, BAP1, UCHL1, UCHL3, UCHL5, ATXN3, ATXN3L, OTUB1, OTUB2, MINDY1, MINDY2, MINDY3, MINDY4, and ZUP1. Exemplary deubiquitinases for use in the present disclosure are also disclosed in Komander, D. et al. Breaking the chains: structure and function of the deubiquitinases. Nat Rev Mol Cell Biol 10, 550–563 (2009), the entire contents of which is incorporated by reference herein.

[00201] In some embodiments, the deubiquitinase is selected from the group consisting of USP1, USP2, USP3, USP4, USP5, USP6, USP7, USP8, USP9X, USP9Y, USP10, USP11, USP12,

USP13, USP14, USP15, USP16, USP17, USP17L2, USP17L3, USP17L4, USP17L5, USP17L7, USP17L8, USP18, USP19, USP20, USP21, USP22, USP23, USP24, USP25, USP26, USP27X, USP28, USP29, USP30, USP31, USP32, USP33, USP34, USP35, USP36, USP37, USP38, USP39, USP40, USP41, USP42, USP43, USP44, USP45, and USP46.

[00202] In some embodiments, the deubiquitinase is BAP1, UCHL1, UCHL3, or UCHL5. In some embodiments, the deubiquitinase is ATXN3 or ATXN3L. In some embodiments, the deubiquitinase is OTUB1 or OTUB2. In some embodiments, the deubiquitinase is MINDY1, MINDY2, MINDY3, or MINDY4. In some embodiments, the deubiquitinase is ZUP1. In some embodiments, the deubiquitinase is a Jab1/Mov34/Mpr1 Pad1 N-terminal+ (MPN+) (JAMM) domain protease.

[00203] In some embodiments, the deubiquitinase is a deubiquitinase described in Table 1. In some embodiments, the amino acid sequence of the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of a deubiquitinase in Table 1. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a catalytic domain of a deubiquitinase in Table 1. In some embodiments, the effector domain comprises a functional fragment of a deubiquitinase in Table 1. In some embodiments, the effector domain deubiquitinase comprises a functional variant of deubiquitinase in Table 1. In some embodiments, the catalytic domain comprises a functional fragment of a catalytic domain of a deubiquitinase in Table 1. In some embodiments, the catalytic domain comprises a functional variant of a catalytic domain of a deubiquitinase in Table 1.

[00204] In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical any one of SEQ ID NOS: 1-112. In some embodiments, the deubiquitinase consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical any one of SEQ ID NOS: 1-112.

[00205] In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%,

97%, 98%, 99%, or 100% identical to SEQ ID NO: 1. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 4. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 5. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 6. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 7. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 8. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 9. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 10. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 11. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 12. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 13. In some embodiments, the deubiquitinase comprises an amino

acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 14. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 15. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 16. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 17. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 18. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 19. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 20. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 21. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 22. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 23. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 24. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 25. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 26. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 27. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 28. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 29. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 30. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 31. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 32. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 33. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 34. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 35. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 36. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 37. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 38. In some

embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 39. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 40. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 41. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 42. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 43. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 44. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 45. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 46. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 47. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 48. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 49. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 50. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%,

84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 51. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 52. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 53. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 54. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 55. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 56. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 57. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 58. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 59. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 60. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 61. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 62. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or

100% identical to SEQ ID NO: 63. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 64. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 65. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 66. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 67. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 68. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 69. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 70. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 71. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 72. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 73. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 74. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 75. In some embodiments, the deubiquitinase comprises an amino

acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 76. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 77. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 78. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 79. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 80. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 81. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 82. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 83. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 84. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 85. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 86. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 87. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 88. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 89. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 90. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 91. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 92. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 93. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 94. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 95. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 96. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 97. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 98. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 99. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 100. In some

embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 101. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 102. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 103. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 104. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 105. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 106. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 107. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 108. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 109. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 110. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 111. In some embodiments, the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 112.

[00206] In some embodiments, the amino acid sequence of the effector domain comprises an

amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of any one of SEQ ID NOS: 1-112. In some embodiments, the amino acid sequence of the effector domain consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of any one of SEQ ID NOS: 1-112.

[00207] In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 1. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 2. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 3. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 4. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 5. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 6. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 7. In some embodiments, the amino acid sequence of the effector domain

comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 8. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 9. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 10. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 11. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 12. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 13. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 14. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 15. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 16. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%,

89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 17. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 18. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 19. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 20. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 21. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 22. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 23. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 24. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 25. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino

acid sequence of the catalytic domain of SEQ ID NO: 26. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 27. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 28. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 29. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 30. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 31. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 32. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 33. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 34. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 35. In some embodiments, the amino acid

sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 36. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 37. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 38. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 39. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 40. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 41. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 42. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 43. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 44. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%,

84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 45. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 46. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 47. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 48. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 49. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 50. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 51. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 52. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 53. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or

100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 54. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 55. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 56. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 57. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 58. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 59. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 60. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 61. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 62. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 63. In some

embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 64. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 65. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 66. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 67. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 68. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 69. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 70. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 71. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 72. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence

at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 73. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 74. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 75. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 76. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 77. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 78. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 79. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 80. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 81. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%,

95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 82. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 83. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 84. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 85. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 86. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 87. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 88. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 89. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 90. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain

of SEQ ID NO: 91. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 92. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 93. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 94. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 95. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 96. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 97. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 98. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 99. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 100. In some embodiments, the amino acid sequence of the effector domain

comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 101. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 102. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 103. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 104. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 105. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 106. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 107. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 108. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 109. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%,

89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 110. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 111. In some embodiments, the amino acid sequence of the effector domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of the catalytic domain of SEQ ID NO: 112.

[00208] In some embodiments, the catalytic domain is derived from a deubiquitinase that comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 1-112. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 1-112.

[00209] In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 1. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 2. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 3. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 4. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%,

94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 6. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 7. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 8. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 9. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 11. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 12. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 13. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 14. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%,

81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 15. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 16. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 17. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 18. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 19. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 20. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 21. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 22. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 23. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 24. In some embodiments, the catalytic

domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 25. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 26. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 27. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 28. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 29. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 30. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 31. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 32. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 33. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%

identical to the amino acid sequence of SEQ ID NO: 34. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 35. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 36. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 37. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 38. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 39. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 40. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 41. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 42. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 43. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%,

85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 44. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 45. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 46. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 47. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 48. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 49. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 50. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 51. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 52. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 53. In some embodiments, the catalytic domain is derived

from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 54. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 55. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 57. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 58. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 59. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 60. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 61. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 62. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the

amino acid sequence of SEQ ID NO: 63. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 64. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 65. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 66. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 67. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 68. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 69. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 70. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 71. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 72. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%,

88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 73. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 74. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 75. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 76. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 77. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 78. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 79. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 80. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 81. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 82. In some embodiments, the catalytic domain is derived from a deubiquitinase

that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 83. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 84. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 85. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 86. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 87. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 88. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 89. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 90. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 91. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence

of SEQ ID NO: 92. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 93. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 94. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 95. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 96. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 97. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 98. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 99. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 100. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 101. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%,

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 102. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 102. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 104. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 105. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 106. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 107. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 108. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 109. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 110. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 111. In some embodiments, the catalytic domain is derived from a deubiquitinase that consists of

an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 112.

[00210] In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 113-220 or 293. In some embodiments, the catalytic domain consists of an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 113-220.

[00211] In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 113. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 114. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 115. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 116. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 117. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 118. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 119. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%,

86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 120. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 121. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 122. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 123. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 124. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 125. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 126. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 127. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 128. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 129. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 130. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%,

89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 131. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 132. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 133. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 134. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 135. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 136. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 137. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 138. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 139. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 140. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 141. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%,

92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 142. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 143. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 144. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 145. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 146. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 147. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 148. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 149. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 150. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 151. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 152. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%,

95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 153. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 154. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 155. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 156. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 157. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 158. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 159. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 160. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 161. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 162. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 163. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%,

99%, or 100% identical to the amino acid sequence of SEQ ID NO: 164. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 165. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 166. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 167. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 168. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 169. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 170. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 171. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 172. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 173. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 174. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical

to the amino acid sequence of SEQ ID NO: 175. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 176. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 177. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 178. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 179. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 180. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 181. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 182. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 183. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 184. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 185. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino

acid sequence of SEQ ID NO: 186. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 187. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 188. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 189. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 190. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 191. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 192. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 193. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 194. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 195. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 196. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of

SEQ ID NO: 197. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 198. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 199. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 200. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 201. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 202. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 203. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 204. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 205. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 206. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 207. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 208.

In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 209. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 210. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 211. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 212. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 213. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 214. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 215. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 216. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 217. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 218. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 219. In some embodiments,

the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 220. In some embodiments, the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 293.

[00212] Table 1 below describes, the amino acid sequence of exemplary human deubiquitinases and exemplary catalytic domains of the exemplary human deubiquitinases. The catalytic domains are exemplary. A person of ordinary skill in the art could readily determine a sufficient amino acid sequence of a human deubiquitinase to mediate deubiquitination (e.g., a catalytic domain). Any of the human deubiquitinases (functional fragment or variants thereof) may be used to derive a catalytic domain for use in a fusion protein described herein.

Table 1. The amino acid sequence of exemplary human deubiquitinases and exemplary catalytic domains of the same

Description	SEQ ID NO	Amino Acid Sequence	SEQ ID NO	Exemplary Catalytic Domains (Amino Acid Sequence)
UBP27_HUMAN Ubiquitin carboxyl-terminal hydrolase 27	1	MCKDYVYDKDIEQIAKEEQGEALKLQASTSTEVSHQQCSVPGLGEKFPTWETTKPELELLGHNPRRRRITSSFTIGLRGLINLGNTCFMNCIVQALTHTPILRDFFLSDRHRCEMPSPELCLVCEMSSLFRELYSGNPSPHVPYKLLHLVWIHARHLAGYRQQDAHEFLIAALDVLHRHCKGDDVGKAANNPNHCNCIIDQIFTGGLQSDVTCQACHGVSTTIDPCWDISLDLPGSCTSFWPMSPGRESSVNGESHIPGITTLTDCLRRFTRPEHLGSSAKIKCGSCQSYQESTKQLTMNKLPVVACFHFKRFEHSAKQRRKITTYISFPLELDMTPFMASSKESRMNGQLQLPTNSGNNENKYSLFAVVNHQGTLESGHYTSFIRHHKDQWFKCDDAVITKASIKDVLDSEGYLLFYHKQVLEHESEKVKEMNTQAY	113	SSFTIGLRGLINLGNTCFMNCIVQALTHTPILRDFFLSDRHRCEMPSPELCLVCEMSSLFRELYSGNPSPHVPYKLLHLVWIHARHLAGYRQQDAHEFLIAALDVLHRHCKGDDVGKAANNPNHCNCIIDQIFTGGLQSDVTCQACHGVSTTIDPCWDISLDLPGSCTSFWPMSPGRESSVNGESHIPGITTLTDCLRRFTRPEHLGSSAKIKCGSCQSYQESTKQLTMNKLPVVACFHFKRFEHSAKQRRKITTYISFPLELDMTPFMASSKESRMNGQLQLPTNSGNNENKYSLFAVVNHQGTLESGHYTSFIRHHKDQWFKCDDAVITKASIKDVLDSEGYLLFYHKQVLEHESEKVKEMNTQAY
UBP48_HUMAN Ubiquitin carboxyl-terminal hydrolase 48	2	MAPRLQLEKAAWRWAETVRPEEVSQEHIETAYRIWLEPCIRGVCRRNCKGNPNCLVGIGEHIWLGEIDENSFHNIDDPNCERRKKNSFVGLTNLGATCYVNTFLQVWFLNLELRQALYLCPSTCSDYMLGDG	114	NSFHNIDDPNCERRKKNSFVGLTNLGATCYVNTFLQVWFLNLELRQALYLCPSTCSDYMLGDGIQEEKDYEPQTICEHLQYLFALLQNSNRRYIDPSGFVKALGLDTGQQQDAQEFSKLF

		IQEEKDYEPQTICEHLQYLFAL LQNSNRRYIDPSGFVKALGLDT GQQQDAQEFSKLFMSLLEDTLS KQKNPDVRNIVQQQFCGEYAYV TVCNQCGRESKLLSKFYELELN IQGHKQLTDCISEFLKEEKLEG DNRYFCENCQSKQNATRKIRLL SLPCTLNLQLMRFVFDRQTGHK KKLNTYIGFSEILDMEPYVEHK GGSYVYELSAVLIHRGVSAYSG HYIAHVKDPQSGEWYKFNDEDI EKMEGKKLQLGIEEDLAEPSKS QTRKPKCGKGTHCSRNAYMLVY RLQTQEKPNTTVQVPAFLQELV DRDNSKFEEWCIEMAEMRKQSV DKGKAKHEEVKELYQRLPAGAE PYEFVSLEWLQKWLDESTPTKP IDNHACLCSHDKLHPDKISIMK RISEYAADIFYSRYGGGPRLTV KALCKECVVERCRILRLKNQLN EDYKTVNNLLKAAVKGSDGFWV GKSSLRSWRQLALEQLDEQDGD AEQSNGKMNGSTLNKDESKEER KEEEELNFNEDILCPHGELCIS ENERRLVSKEAWSKLQQYFPKA PEFPSYKECCSQCKILEREGEE NEALHKMIANEQKTSLPNLFQD KNRPCLSNWPEDTDVLYIVSQF FVEEWRKFVRKPTRCSPVSSVG NSALLCPHGGLMFTFASMTKED SKLIALIWPSEWQMIQKLFVVD HVIKITRIEVGDVNPSETQYIS EPKLCPECREGLLCQQQRDLRE YTQATIYVHKVVDNKKVMKDSA PELNVSSSETEEDKEEAKPDGE KDPDFNQSNGGTKRQKISHQNY IAYQKQVIRRSMRHRKVRGEKA LLVSANQTLKELKIQIMHAFSV APFDQNLSIDGKILSDDCATLG TLGVIPESVILLKADEPIADYA AMDDVMQVCMPEEGFKGTGLLG H		MSLLEDTLSKQKNPDVRNIV QQQFCGEYAYVTVCNQCGRE SKLLSKFYELELNIQGHKQL TDCISEFLKEEKLEGDNRYF CENCQSKQNATRKIRLLSLP CTLNLQLMRFVFDRQTGHKK KLNTYIGFSEILDMEPYVEH KGGSYVYELSAVLIHRGVSA YSGHYIAHVKDPQSGEWYKF NDEDIEKMEGKKLQLGIEED LAEPSKSQTRKPKCGKGTHC SRNAYMLVYRLQT
UBP3_HUMAN Ubiquitin carboxyl-terminal hydrolase 3	3	MECPHLSSSVCIAPDSAKFPNG SPSSWCCSVCRSNKSPWVCLTC SSVHCGRYVNGHAKKHYEDAQV PLTNHKKSEKQDKVQHTVCMDC SSYSTYCYRCDDFVVNDTKLGL VQKVREHLQNLENSAFTADRHK KRKLLENSTLNSKLLKVNGSTT AICATGLRNLGNTCFMNAILQS LSNIEQFCCYFKELPAVELRNG	115	TAICATGLRNLGNTCFMNAI LQSLSNIEQFCCYFKELPAV ELRNGKTAGRRTYHTRSQGD NNVSLVEEFRKTLCALWQGS QTAFSPESLFYVVWKIMPNF RGYQQQDAHEFMRYLLDHLH LELQGGFNGVSRSAILQENS TLSASNKCCINGASTVVTAI FGGILQNEVNCLICGTESRK

		KTAGRRTYHTRSQGDNNVSLVE EFRKTLCALWQGSQTAFSPESL FYVVWKIMPNFRGYQQQDAHEF MRYLLDHLHLELQGGFNGVSRS AILQENSTLSASNKCCINGAST VVTAIFGGILQNEVNCLICGTE SRKFDPFLDLSLDIPSQFRSKR SKNQENGPVCSLRDCLRSFTDL EELDETELYMCHKCKKKQKSTK KFWIQKLPKVLCLHLKRFHWTA YLRNKVDTYVEFPLRGLDMKCY LLEPENSGPESCLYDLAAVVVH HGSGVGSGHYTAYATHEGRWFH FNDSTVTLTDEETVVKAKAYIL FYVEHQAKAGSDKL		FDPFLDLSLDIPSQFRSKRS KNQENGPVCSLRDCLRSFTD LEELDETELYMCHKCKKKQK STKKFWIQKLPKVLCLHLKR FHWTAYLRNKVDTYVEFPLR GLDMKCYLLEPENSGPESCL YDLAAVVVHHGSGVGSGHYT AYATHEGRWFHFNDSTVTLT DEETVVKAKAYILFYVEHQ
U17LB_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 11	4	QLAPREKLPLSSRRPAAVGAGL QNMGNTCYVNASLQCLTYTPPL ANYMLSREHSQTCHRHKGCMLC TMQAHITRALHNPGHVIQPSQA LAAGFHRGKQEDAHEFLMFTVD AMKKACLPGHKQVDHHSKDTTL IHQIFGGYWRSQIKCLHCHGIS DTFDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGVCL QRAPASKTLTLHTSAKVLILVL KRFSDVTGNKIAKNVQYPECLD MQPYMSQTNTGPLVYVLYAVLV HAGWSCHNGHYFSYVKAQEGQW YKMDDAEVTASSITSVLSQQAY VLFYIQKSEWERHSESVSRGRE PRALGAEDTDRRATQGELKRDH PCLQAPELDEHLVERATQESTL DHWKFLQEQNKTKPEFNVRKVE GTLPPDVLVIHQSKYKCGMKNH HPEQQSSLLNLSSTTPTHQESM NTGTLASLRGRARRSKGKNKHS KRALLVCQ	116	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQTNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS
UBP1_HUMAN Ubiquitin carboxyl-terminal hydrolase 1	5	MPGVIPSESNGLSRGSPSKKNR LSLKFFQKKETKRALDFTDSQE NEEKASEYRASEIDQVVPAAQS SPINCEKRENLLPFVGLNNLGN TCYLNSILQVLYFCPGFKSGVK HLFNIISRKKEALKDEANQKDK GNCKEDSLASYELICSLQSLII SVEQLQASFLLNPEKYTDELAT QPRRLLNTLRELNPMYEGYLQH DAQEVLQCILGNIQETCQLLKK EEVKNVAELPTKVEEIPHPKEE MNGINSIEMDSMRHSEDFKEKL PKGNGKRKSDTEFGNMKKKVKL SKEHQSLEENQRQTRSKRKATS	117	LPFVGLNNLGNTCYLNSILQ VLYFCPGFKSGVKHLFNIIS RKKEALKDEANQKDKGNCKE DSLASYELICSLQSLIISVE QLQASFLLNPEKYTDELATQ PRRLLNTLRELNPMYEGYLQ HDAQEVLQCILGNIQETCQL LKKEEVKNVAELPTKVEEIP HPKEEMNGINSIEMDSMRHS EDFKEKLPKGNGKRKSDTEF GNMKKKVKLSKEHQSLEENQ RQTRSKRKATSDTLESPPKI IPKYISENESPRPSQKKSRV KINWLKSATKQPSILSKFCS

		DTLESPPKIIPKYISENESPRP SQKKSRVKINWLKSATKQPSIL SKFCSLGKITTNQGVKGQSKEN ECDPEEDLGKCESDNTTNGCGL ESPGNTVTPVNVNEVKPINKGE EQIGFELVEKLFQGQLVLRTRC LECESLTERREDFQDISVPVQE DELSKVEESSEISPEPKTEMKT LRWAISQFASVERIVGEDKYFC ENCHHYTEAERSLLFDKMPEVI TIHLKCFAASGLEFDCYGGGLS KINTPLLTPLKLSLEEWSTKPT NDSYGLFAVVMHSGITISSGHY TASVKVTDLNSLELDKGNFVVD QMCEIGKPEPLNEEEARGVVEN YNDEEVSIRVGGNTQPSKVLNK KNVEAIGLLGGQKSKADYELYN KASNPDKVASTAFAENRNSETS DTTGTHESDRNKESSDQTGINI SGFENKISYVVQSLKEYEGKWL LFDDSEVKVTEEKDFLNSLSPS TSPTSTPYLLFYKKL		LGKITTNQGVKGQSKENECD PEEDLGKCESDNTTNGCGLE SPGNTVTPVNVNEVKPINKG EEQIGFELVEKLFQGQLVLR TRCLECESLTERREDFQDIS VPVQEDELSKVEESSEISPE PKTEMKTLRWAISQFASVER IVGEDKYFCENCHHYTEAER SLLFDKMPEVITIHLKCFAA SGLEFDCYGGGLSKINTPLL TPLKLSLEEWSTKPTNDSYG LFAVVMHSGITISSGHYTAS VKVTDLNSLELDKGNFVVDQ MCEIGKPEPLNEEEARGVVE NYNDEEVSIRVGGNTQPSKV LNKKNVEAIGLLGGQKSKAD YELYNKASNPDKVASTAFAE NRNSETSDTTGTHESDRNKE SSDQTGINISGFENKISYVV QSLKEYEGKWLLFDDSEVKV TEEKDFLNSLSPSTSPTSTP YLLFYKKL
UBP40_HUMAN Ubiquitin carboxyl-terminal hydrolase 40	6	MFGDLFEEEYSTVSNNQYGKGK KLKTKALEPPAPREFTNLSGIR NQGGTCYLNSLLQTLHFTPEFR EALFSLGPEELGLFEDKDKPDA KVRIIPLQLQRLFAQLLLLDQE AASTADLTDSFGWTSNEEMRQH DVQELNRILFSALETSLVGTSG HDLIYRLYHGTIVNQIVCKECK NVSERQEDFLDLTVAVKNVSGL EDALWNMYVEEEVFDCDNLYHC GTCDRLVKAAKSAKLRKLPPFL TVSLLRFNFDFVKCERYKETSC YTFPLRINLKPFCEQSELDDLE YIYDLFSVIIHKGGCYGGHYHV YIKDVDHLGNWQFQEEKSKPDV NLKDLQSEEEIDHPLMILKAIL LEENNLIPVDQLGQKLLKKIGI SWNKKYRKQHGPLRKFLQLHSQ IFLLSSDESTVRLLKNSSLQAE SDFQRNDQQIFKMLPPESPGLN NSISCPHWFDINDSKVQPIREK DIEQQFQGKESAYMLFYRKSQL QRPPEARANPRYGVPCHLLNEM DAANIELQTKRAECDSANNTFE LHLHLGPQYHFFNGALHPVVSQ TESVWDLTFDKRKTLGDLRQSI FQLLEFWEGDMVLSVAKLVPAG LHIYQSLGGDELTLCETEIADG EDIFVWNGVEVGGVHIQTGIDC	118	FTNLSGIRNQGGTCYLNSLL QTLHFTPEFREALFSLGPEE LGLFEDKDKPDAKVRIIPLQ LQRLFAQLLLLDQEAASTAD LTDSFGWTSNEEMRQHDVQE LNRILFSALETSLVGTSGHD LIYRLYHGTIVNQIVCKECK NVSERQEDFLDLTVAVKNVS GLEDALWNMYVEEEVFDCDN LYHCGTCDRLVKAAKSAKLR KLPPFLTVSLLRFNFDFVKC ERYKETSCYTFPLRINLKPF CEQSELDDLEYIYDLFSVII HKGG CYGGHYHVYIKDVDHLGNWQ FQEEKSKPDVNLKDLQSEEE IDHPLMILKAILLEENNLIP VDQLGQKLLKKIGISWNKKY RKQHGPLRKFLQLHSQIFLL SSDESTVRLLKNSSLQAESD FQRNDQQIFKMLPPESPGLN NSISCPHWFDINDSKVQPIR EKDIEQQFQGKESAYMLFYR KSQLQRPPEARANPRYGVPC HLLNEMDAANIELQTKRAEC DSANNTFELHLHLGPQYHFF NGALHPVVSQTESVWDLTFD KRKTLGDLRQSIFQLLEFWE GDMVLSVAKLVPAGLHIYQS

		EPLLLNVLHLDTSSDGEKCCQV IESPHVFPANAEVGTVLTALAI PAGVIFINSAGCPGGEGWTAIP KEDMRKTFREQGLRNGSSILIQ DSHDDNSLLTKEEKWVTSMNEI DWLHVKNLCQLESEEKQVKISA TVNTMVFDIRIKAIKELKLMKE LADNSCLRPIDRNGKLLCPVPD SYTLKEAELKMGSSLGLCLGKA PSSSQLFLFFAMGSDVQPGTEM EIVVEETISVRDCLKLMLKKSG LQGDAWHLRKMDWCYEAGEPLC EEDATLKELLICSGDTLLLIEG QLPPLGFLKVPIWWYQLQGPSG HWESHQDQTNCTSSWGRVWRAT SSQGASGNEPAQVSLLYLGDIE ISEDATLAELKSQAMTLPPFLE FGVPSPAHLRAWTVERKRPGRL LRTDRQPLREYKLGRRIEICLE PLQKGENLGPQDVLLRTQVRIP GERTYAPALDLVWNAAQGGTAG SLRQRVADFYRLPVEKIEIAKY FPEKFEWLPISSWNQQITKRKK KKKQDYLQGAPYYLKDGDTIGV KNLLIDDDDDFSTIRDDTGKEK QKQRALGRRKSQEALHEQSSYI LSSAETPARPRAPETSLSIHVG SFR		LGGDELTLCETEIADGEDIF VWNGVEVGGVHIQTGIDCEP LLLNVLHLDTSSDGEKCCQV IESPHVFPANAEVGTVLTAL AIPAGVIFINSAGCPGGEGW TAIPKEDMRKTFREQGLRNG SSILIQDSHDDNSLLTKEEK WVTSMNEIDWLHVKNLCQLE SEEKQVKISATVNTMVFDIR IKAIKELKLMKELADNSCLR PIDRNGKLLCPVPDSYTLKE AELKMGSSLGLCLGKAPSSS QLFLFFAMGSDVQPGTEMEI VVEETISVRDCLKLMLKKSG LQGDAWHLRKMDWCYEAGEP LCEEDATLKELLICSGDTLL LIEGQLPPLGFLKVPIWWYQ LQGPSGHWESHQDQTNCTSS WGRVWRATSSQGASGNEPAQ VSLLYLGDIEISEDATLAEL KSQAMTLPPFLEFGVPSPAH LRAWTVERKRPGRLLRTDRQ PLREYKLGRRIEICLEPLQK GENLGPQDVLLRTQVRIPGE RTYAPALDLVWNAAQGGTAG SLRQRVADFYRLPVEKIEIA KYFPEKFEWLPISSWNQQIT KRKKKKKQDYLQGAPYYLKD GDTIGVKNLLIDDDDDFSTI RDDTGKEKQKQRALGRRKSQ
UBP7_HUMAN Ubiquitin carboxyl-terminal hydrolase 7	7	MNHQQQQQQQKAGEQQLSEPED MEMEAGDTDDPPRITQNPVING NVALSDGHNTAEEDMEDDTSWR SEATFQFTVERFSRLSESVLSP PCFVRNLPWKIMVMPRFYPDRP HQKSVGFFLQCNAESDSTSWSC HAQAVLKIINYRDDEKSFSRRI SHLFFHKENDWGFSNFMAWSEV TDPEKGFIDDDKVTFEVFVQAD APHGVAWDSKKHTGYVGLKNQG ATCYMNSLLQTLFFTNQLRKAV YMMPTEGDDSSKSVPLALQRVF YELQHSDKPVGTKKLTKSFGWE TLDSFMQHDVQELCRVLLDNVE NKMKGTCVEGTIPKLFRGKMVS YIQCKEVDYRSDRREDYYDIQL SIKGKKNIFESFVDYVAVEQLD GDNKYDAGEHGLQEAEKGVKFL TLPPVLHLQLMRFMYDPQTDQN IKINDRFEFPEQLPLDEFLQKT DPKDPANYILHAVLVHSGDNHG	119	TGYVGLKNQGATCYMNSLLQ TLFFTNQLRKAVYMMPTEGD DSSKSVPLALQRVFYELQHS DKPVGTKKLTKSFGWETLDS FMQHDVQELCRVLLDNVENK MKGTCVEGTIPKLFRGKMVS YIQCKEVDYRSDRREDYYDI QLSIKGKKNIFESFVDYVAV EQLDGDNKYDAGEHGLQEAE KGVKFLTLPPVLHLQLMRFM YDPQTDQNIKINDRFEFPEQ LPLDEFLQKTDPKDPANYIL HAVLVHSGDNHGGHYVVYLN PKGDGKWCKFDDDVVSRCTK EEAIEHNYGGHDDDLSVRHC TNAYMLVYIRE

		GHYVVYLNPKGDGKWCKFDDDV VSRCTKEEAIEHNYGGHDDDLS VRHCTNAYMLVYIRESKLSEVL QAVTDHDIPQQLVERLQEEKRI EAQKRKERQEAHLYMQVQIVAE DQFCGHQGNDMYDEEKVKYTVF KVLKNSSLAEFVQSLSQTMGFP QDQIRLWPMQARSNGTKRPAML DNEADGNKTMIELSDNENPWTI FLETVDPELAASGATLPKFDKD HDVMLFLKMYDPKTRSLNYCGH IYTPISCKIRDLLPVMCDRAGF IQDTSLILYEEVKPNLTERIQD YDVSLDKALDELMDGDIIVFQK DDPENDNSELPTAKEYFRDLYH RVDVIFCDKTIPNDPGFVVTLS NRMNYFQVAKTVAQRLNTDPML LQFFKSQGYRDGPGNPLRHNYE GTLRDLLQFFKPRQPKKLYYQQ LKMKITDFENRRSFKCIWLNSQ FREEEITLYPDKHGCVRDLLEE CKKAVELGEKASGKLRLLEIVS YKIIGVHQEDELLECLSPATSR TFRIEEIPLDQVDIDKENEMLV TVAHFHKEVFGTFGIPFLLRIH QGEHFREVMKRIQSLLDIQEKE FEKFKFAIVMMGRHQYINEDEY EVNLKDFEPQPGNMSHPRPWLG LDHFNKAPKRSRYTYLEKAIKI HN		
U17L5_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 5	8	MEDDSLYLRGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLAK PEELNGENAYHCGVCLQRAPAS KTLTLHTSAKVLILVLKRFSDV TGNKIAKNVQYPECLDMQPYMS QPNTGPLVYVLYAVLVHAGWSC HNGHYFSYVKAQEGQWYKMDDA EVTASSITSVLSQQAYVLFYIQ KSEWERHSESVSRGREPRALGA EDTDRRATQGELKRDHPCLQAP ELDEHLVERATQESTLDHWKFL QEQNKTKPEFNVRKVEGTLPPD	120	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLAKPEELNGENAYHCGV CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQPNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS EWERHSESVSRGREPRALGA EDTDRRATQGELKRDHPCLQ APEL

		VLVIHQSKYKCGMKNHHPEQQS SLLNLSSSTPTHQESMNTGTLA SLRGRARRSKGKNKHSKRALLV CQ		
U17LL_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 21	9	MEEDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE KLPLSNRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KMLTLLTSAKVLILVLKRFSDV TGNKIAKNVQYPECLDMQPYMS QPNTGPLVYVLYAVLVHAGWSC HNGHYFSYVKAQEGQWYKMDDA EVTASSITSVLSQQAYVLFYIQ KSEWERHSESVSRGREPRALGA EDTDRRATQGELKRDHPCLQAP ELDEHLVERATQESTLDHWKFL QEQNKTKPEFNVRKVEGTLPPD VLVIHQSKYKCGMKNHHPEQQS SLLNLSSSTPTHQESMNTGTLA SLRGRARRSKGKNKHSKRALLV CQ	121	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKMLTLLTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQPNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS EWERHSESVSRGREPRALGA EDTDRRATQGELKRDHPCLQ APEL
U17LA_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 10	10	MEDDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE KPPLSSRRPAAVGAGLQNMGNT CYVNASLQCLTYKPPLANYMLF REHSQTCHRHKGCMLCTMQAHI TRALHIPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMRKAC LPGHKQVDRHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KTLTLHNSAKVLILVLKRFPDV TGNKIAKNVQYPECLDMQPYMS QQNTGPLVYVLYAVLVHAGWSC HNGHYSSYVKAQEGQWYKMDDA EVTASSITSVLSQQAYVLFYIQ KSEWERHSESVSRGREPRALGV EDTDRRATQGELKRDHPCLQAP ELDEHLVERATQESTLDHWKFL QEQNKTKPEFNVRRVEGTVPPD VLVIHQSKYKCRMKNHHPEQQS	122	AVGAGLQNMGNTCYVNASLQ CLTYKPPLANYMLFREHSQT CHRHKGCMLCTMQAHITRAL HIPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMRKAC LPGHKQVDRHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKTLTLHNSAKVL ILVLKRFPDVTGNKIAKNVQ YPECLDMQPYMSQQNTGPLV YVLYAVLVHAGWSCHNGHYS SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS EWERHSESVSRGREPRALGV EDTDRRATQGELKRDHPCLQ APEL

		SLLNLSSTTPTDQESMNTGTLA SLRGRTRRSKGKNKHSKRALLV CQ		
UBP41_HUMAN Putative ubiquitin carboxyl-terminal hydrolase 41	11	MDGVLFRAHQCQYVHPCVHVYV TVGLMDPLCERKEKASKQEREN PLAHLAAWGLVGLHNIGQTCCL NSLIQVFVMNVDFARILKRITV PRGADEQRRSVPFQMLLLLEKM QDSRQKAVWPLELAYCLQKYNV PLFVQHDAAQLYLKLWNLIKDQ IADVHLVERLQALYMIRMKDSL ICLDCAMESSRNSSMLTLRLSF FDVDSKPLKTLEDALHCFFQPR ELSSKSKCFCENCGKKTRGKQV LKLTHLPQTLTIHLMRFSIRNS QTRKICHSLYFPQSLDFSQILP MKRESCDAEEQSGGQYELFAVI AHVGMADSGHYCVYIRNAVDGK WFCFNDSNICLVSWEDIQCTYG NPNYHW	123	WGLVGLHNIGQTCCLNSLIQ VFVMNVDFARILKRITVPRG ADEQRRSVPFQMLLLLEKMQ DSRQKAVWPLELAYCLQKYN VPLFVQHDAAQLYLKLWNLI KDQIADVHLVERLQALYMIR MKDSLICLDCAMESSRNSSM LTLRLSFFDVDSKPLKTLED ALHCFFQPRELSSKSKCFCE NCGKKTRGKQVLKLTHLPQT LTIHLMRFSIRNSQTRKICH SLYFPQSLDFSQILPMKRES CDAEEQSGGQYELFAVIAHV GMADSGHYCVYIRNAVDGKW FCFNDSNICLVSWEDIQCTY GNPNYHW
UBP38_HUMAN Ubiquitin carboxyl-terminal hydrolase 38	12	MDKILEGLVSSSHPLPLKRVIV RKVVESAEHWLDEAQCEAMFDL TTRLILEGQDPFQRQVGHQVLE AYARYHRPEFESFFNKTFVLGL LHQGYHSLDRKDVAILDYIHNG LKLIMSCPSVLDLFSLLQVEVL RMVCERPEPQLCARLSDLLTDF VQCIPKGKLSITFCQQLVRTIG HFQCVSTQERELREYVSQVTKV SNLLQNIWKAEPATLLPSLQEV FASISSTDASFEPSVALASLVQ HIPLQMITVLIRSLTTDPNVKD ASMTQALCRMIDWLSWPLAQHV DTWVIALLKGLAAVQKFTILID VTLLKIELVFNRLWFPLVRPGA LAVLSHMLLSFQHSPEAFHLIV PHVVNLVHSFKNDGLPSSTAFL VQLTELIHCMMYHYSGFPDLYE PILEAIKDFPKPSEEKIKLILN QSAWTSQSNSLASCLSRLSGKS ETGKTGLINLGNTCYMNSVIQA LFMATDFRRQVLSLNLNGCNSL MKKLQHLFAFLAHTQREAYAPR IFFEASRPPWFTPRSQQDCSEY LRFLLDRLHEEEKILKVQASHK PSEILECSETSLQEVASKAAVL TETPRTSDGEKTLIEKMFGGKL RTHIRCLNCRSTSQKVEAFTDL SLAFCPSSSLENMSVQDPASSP SIQDGGLMQASVPGPSEEPVVY NPTTAAFICDSLVNEKTIGSPP	124	SETGKTGLINLGNTCYMNSV IQALFMATDFRRQVLSLNLN GCNSLMKKLQHLFAFLAHTQ REAYAPRIFFEASRPPWFTP RSQQDCSEYLRFLLDRLHEE EKILKVQASHKPSEILECSE TSLQEVASKAAVLTETPRTS DGEKTLIEKMFGGKLRTHIR CLNCRSTSQKVEAFTDLSLA FCPSSSLENMSVQDPASSPS IQDGGLMQASVPGPSEEPVV YNPTTAAFICDSLVNEKTIG SPPNEFYCSENTSVPNESNK ILVNKDVPQKPGGETTPSVT DLLNYFLAPEILTGDNQYYC ENCASLQNAEKTMQITEEPE YLILTLLRFSYDQKYHVRRK ILDNVSLPLVLELPVKRITS FSSLSESWSVDVDFTDLSEN LAKKLKPSGTDEASCTKLVP YLLSSVVVHSGISSESGHYY SYARNITSTDSSYQMYHQSE ALALASSQSHLLGRDSPSAV FEQDLENKEMSKEWFLFNDS RVTFTSFQSVQKITSRFPKD TAYVLLYKKQH

		NEFYCSENTSVPNESNKILVNK DVPQKPGGETTPSVTDLLNYFL APEILTGDNQYYCENCASLQNA EKTMQITEEPEYLILTLLRFSY DQKYHVRRKILDNVSLPLVLEL PVKRITSFSSLSESWSVDVDFT DLSENLAKKLKPSGTDEASCTK LVPYLLSSVVVHSGISSESGHY YSYARNITSTDSSYQMYHQSEA LALASSQSHLLGRDSPSAVFEQ DLENKEMSKEWFLFNDSRVTFT SFQSVQKITSRFPKDTAYVLLY KKQHSTNGLSGNNPTSGLWING DPPLQKELMDAITKDNKLYLQE QELNARARALQAASASCSFRPN GFDDNDPPGSCGPTGGGGGGGF NTVGRLVF		
UBP43_HUMAN Ubiquitin carboxyl-terminal hydrolase 43	13	MDLGPGDAAGGGPLAPRPRRRR SLRRLFSRFLLALGSRSRPGDS PPRPQPGHCDGDGEGGFACAPG PVPAAPGSPGEERPPGPQPQLQ LPAGDGARPPGAQGLKNHGNTC FMNAVVQCLSNTDLLAEFLALG RYRAAPGRAEVTEQLAALVRAL WTREYTPQLSAEFKNAVSKYGS QFQGNSQHDALEFLLWLLDRVH EDLEGSSRGPVSEKLPPEATKT SENCLSPSAQLPLGQSFVQSHF QAQYRSSLTCPHCLKQSNTFDP FLCVSLPIPLRQTRFLSVTLVF PSKSQRFLRVGLAVPILSTVAA LRKMVAEEGGVPADEVILVELY PSGFQRSFFDEEDLNTIAEGDN VYAFQVPPSPSQGTLSAHPLGL SASPRLAAREGQRFSLSLHSES KVLILFCNLVGSGQQASRFGPP FLIREDRAVSWAQLQQSILSKV RHLMKSEAPVQNLGSLFSIRVV GLSVACSYLSPKDSRPLCHWAV DRVLHLRRPGGPPHVKLAVEWD SSVKERLFGSLQEERAQDADSV WQQQQAHQQHSCTLDECFQFYT KEEQLAQDDAWKCPHCQVLQQG MVKLSLWTLPDILIIHLKRFCQ VGERRNKLSTLVKFPLSGLNMA PHVAQRSTSPEAGLGPWPSWKQ PDCLPTSYPLDFLYDLYAVCNH HGNLQGGHYTAYCRNSLDGQWY SYDDSTVEPLREDEVNTRGAYI LFYQKRNSIPPWSASSSMRGST SSSLSDHWLLRLGSHAGSTRGS	125	RPPGAQGLKNHGNTCFMNAV VQCLSNTDLLAEFLALGRYR AAPGRAEVTEQLAALVRALW TREYTPQLSAEFKNAVSKYG SQFQGNSQHDALEFLLWLLD RVHEDLEGSSRGPVSEKLPP EATKTSENCLSPSAQLPLGQ SFVQSHFQAQYRSSLTCPHC LKQSNTFDPFLCVSLPIPLR QTRFLSVTLVFPSKSQRFLR VGLAVPILSTVAALRKMVAE EGGVPADEVILVELYPSGFQ RSFFDEEDLNTIAEGDNVYA FQVPPSPSQGTLSAHPLGLS ASPRLAAREGQRFSLSLHSE SKVLILFCNLVGSGQQASRF GPPFLIREDRAVSWAQLQQS ILSKVRHLMKSEAPVQNLGS LFSIRVVGLSVACSYLSPKD SRPLCHWAVDRVLHLRRPGG PPHVKLAVEWDSSVKERLFG SLQEERAQDADSVWQQQQAH QQHSCTLDECFQFYTKEEQL AQDDAWKCPHCQVLQQGMVK LSLWTLPDILIIHLKRFCQV GERRNKLSTLVKFPLSGLNM APHVAQRSTSPEAGLGPWPS WKQPDCLPTSYPLDFLYDLY AVCNHHGNLQGGHYTAYCRN SLDGQWYSYDDSTVEPLRED EVNTRGAYILFYQKRN

		LLSWSSAPCPSLPQVPDSPIFT NSLCNQEKGGLEPRRLVRGVKG RSISMKAPTTSRAKQGPFKTMP LRWSFGSKEKPPGASVELVEYL ESRRRPRSTSQSIVSLLTGTAG EDEKSASPRSNVALPANSEDGG RAIERGPAGVPCPSAQPNHCLA PGNSDGPNTARKLKENAGQDIK LPRKFDLPLTVMPSVEHEKPAR PEGQKAMNWKESFQMGSKSSPP SPYMGFSGNSKDSRRGTSELDR PLQGTLTLLRSVFRKKENRRNE RAEVSPQVPPVSLVSGGLSPAM DGQAPGSPPALRIPEGLARGLG SRLERDVWSAPSSLRLPRKASR APRGSALGMSQRTVPGEQASYG TFQRVKYHTLSLGRKKTLPESS F		
UBP2_HUMAN Ubiquitin carboxyl-terminal hydrolase 2	14	MSQLSSTLKRYTESARYTDAHY AKSGYGAYTPSSYGANLAASLL EKEKLGFKPVPTSSFLTRPRTY GPSSLLDYDRGRPLLRPDITGG GKRAESQTRGTERPLGSGLSGG SGFPYGVTNNCLSYLPINAYDQ GVTLTQKLDSQSDLARDFSSLR TSDSYRIDPRNLGRSPMLARTR KELCTLQGLYQTASCPEYLVDY LENYGRKGSASQVPSQAPPSRV PEIISPTYRPIGRYTLWETGKG QAPGPSRSSSPGRDGMNSKSAQ GLAGLRNLGNTCFMNSILQCLS NTRELRDYCLQRLYMRDLHHGS NAHTALVEEFAKLIQTIWTSSP NDVVSPSEFKTQIQRYAPRFVG YNQQDAQEFLRFLLDGLHNEVN RVTLRPKSNPENLDHLPDDEKG RQMWRKYLEREDSRIGDLFVGQ LKSSLTCTDCGYCSTVFDPFWD LSLPIAKRGYPEVTLMDCMRLF TKEDVLDGDEKPTCCRCRGRKR CIKKFSIQRFPKILVLHLKRFS ESRIRTSKLTTFVNFPLRDLDL REFASENTNHAVYNLYAVSNHS GTTMGGHYTAYCRSPGTGEWHT FNDSSVTPMSSSQVRTSDAYLL FYELASPPSRM	126	SAQGLAGLRNLGNTCFMNSI LQCLSNTRELRDYCLQRLYM RDLHHGSNAHTALVEEFAKL IQTIWTSSPNDVVSPSEFKT QIQRYAPRFVGYNQQDAQEF LRFLLDGLHNEVNRVTLRPK SNPENLDHLPDDEKGRQMWR KYLEREDSRIGDLFVGQLKS SLTCTDCGYCSTVFDPFWDL SLPIAKRGYPEVTLMDCMRL FTKEDVLDGDEKPTCCRCRG RKRCIKKFSIQRFPKILVLH LKRFSESRIRTSKLTTFVNF PLRDLDLREFASENTNHAVY NLYAVSNHSGTTMGGHYTAY CRSPGTGEWHTFNDSSVTPM SSSQVRTSDAYLLFYELAS
UBP45_HUMAN Ubiquitin carboxyl-terminal hydrolase 45	15	MRVKDPTKALPEKAKRSKRPTV PHDEDSSDDIAVGLTCQHVSHA ISVNHVKRAIAENLWSVCSECL KERRFYDGQLVLTSDIWLCLKC GFQGCGKNSESQHSLKHFKSSR	127	LSVRGITNLGNTCFFNAVMQ NLAQTYTLTDLMNEIKESST KLKIFPSSDSQLDPLVVELS RPGPLTSALFLFLHSMKETE KGPLSPKVLFNQLCQKAPRF

		TEPHCIIINLSTWIIWCYECDE KLSTHCNKKVLAQIVDFLQKHA SKTQTSAFSRIMKLCEEKCETD EIQKGGKCRNLSVRGITNLGNT CFFNAVMQNLAQTYTLTDLMNE IKESSTKLKIFPSSDSQLDPLV VELSRPGPLTSALFLFLHSMKE TEKGPLSPKVLFNQLCQKAPRF KDFQQQDSQELLHYLLDAVRTE ETKRIQASILKAFNNPTTKTAD DETRKKVKAYGKEGVKMNFIDR IFIGELTSTVMCEECANISTVK DPFIDISLPIIEERVSKPLLWG RMNKYRSLRETDHDRYSGNVTI ENIHQPRAAKKHSSSKDKSQLI HDRKCIRKLSSGETVTYQKNEN LEMNGDSLMFASLMNSESRLNE SPTDDSEKEASHSESNVDADSE PSESESASKQTGLFRSSSGSGV QPDGPLYPLSAGKLLYTKETDS GDKEMAEAISELRLSSTVTGDQ DFDRENQPLNISNNLCFLEGKH LRSYSPQNAFQTLSQSYITTSK ECSIQSCLYQFTSMELLMGNNK LLCENCTKNKQKYQEETSFAEK KVEGVYTNARKQLLISAVPAVL ILHLKRFHQAGLSLRKVNRHVD FPLMLDLAPFCSATCKNASVGD KVLYGLYGIVEHSGSMREGHYT AYVKVRTPSRKLSEHNTKKKNV PGLKAADNESAGQWVHVSDTYL QVVPESRALSAQAYLLFYERVL		KDFQQQDSQELLHYLLDAVR TEETKRIQASILKAFNNPTT KTADDETRKKVKAYGKEGVK MNFIDRIFIGELTSTVMCEE CANISTVKDPFIDISLPIIE ERVSKPLLWGRMNKYRSLRE TDHDRYSGNVTIENIHQPRA AKKHSSSKDKSQLIHDRKCI RKLSSGETVTYQKNENLEMN GDSLMFASLMNSESRLNESP TDDSEKEASHSESNVDADSE PSESESASKQTGLFRSSSGS GVQPDGPLYPLSAGKLLYTK ETDSGDKEMAEAISELRLSS TVTGDQDFDRENQPLNISNN LCFLEGKHLRSYSPQNAFQT LSQSYITTSKECSIQSCLYQ FTSMELLMGNNKLLCENCTK NKQKYQEETSFAEKKVEGVY TNARKQLLISAVPAVLILHL KRFHQAGLSLRKVNRHVDFP LMLDLAPFCSATCKNASVGD KVLYGLYGIVEHSGSMREGH YTAYVKVRTPSRKLSEHNTK KKNVPGLKAADNESAGQWVH VSDTYLQVVPESRALSAQAY LLFYERVL
UBP32_HUMAN Ubiquitin carboxyl-terminal hydrolase 32	16	MGAKESRIGFLSYEEALRRVTD VELKRLKDAFKRTCGLSYYMGQ HCFIREVLGDGVPPKVAEVIYC SFGGTSKGLHFNNLIVGLVLLT RGKDEEKAKYIFSLFSSESGNY VIREEMERMLHVVDGKVPDTLR KCFSEGEKVNYEKFRNWLFLNK DAFTFSRWLLSGGVYVTLTDDS DTPTFYQTLAGVTHLEESDIID LEKRYWLLKAQSRTGRFDLETF GPLVSPPIRPSLSEGLFNAFDE NRDNHIDFKEISCGLSACCRGP LAERQKFCFKVFDVDRDGVLSR VELRDMVVALLEVWKDNRTDDI PELHMDLSDIVEGILNAHDTTK MGHLTLEDYQIWSVKNVLANEF LNLLFQVCHIVLGLRPATPEEE GQIIRGWLERESRYGLQAGHNW FIISMQWWQQWKEYVKYDANPV	128	TEKGATGLSNLGNTCFMNSS IQCVSNTQPLTQYFISGRHL YELNRTNPIGMKGHMAKCYG DLVQELWSGTQKNVAPLKLR WTIAKYAPRFNGFQQQDSQE LLAFLLDGLHEDLNRVHEKP YVELKDSDGRPDWEVAAEAW DNHLRRNRSIVVDLFHGQLR SQVKCKTCGHISVRFDPFNF LSLPLPMDSYMHLEITVIKL DGTTPVRYGLRLNMDEKYTG LKKQLSDLCGLNSEQILLAE VHGSNIKNFPQDNQKVRLSV SGFLCAFEIPVPVSPISASS PTQTDFSSSPSTNEMFTLTT NGDLPRPIFIPNGMPNTVVP CGTEKNFTNGMVNGHMPSLP DSPFTGYIIAVHRKMMRTEL YFLSSQKNRPSLFGMPLIVP

		VIEPSSVLNGGKYSFGTAAHPM EQVEDRIGSSLSYVNTTEEKFS DNISTASEASETAGSGFLYSAT PGADVCFARQHNTSDNNNQCLL GANGNILLHLNPQKPGAIDNQP LVTQEPVKATSLTLEGGRLKRT PQLIHGRDYEMVPEPVWRALYH WYGANLALPRPVIKNSKTDIPE LELFPRYLLFLRQQPATRTQQS NIWVNMGNVPSPNAPLKRVLAY TGCFSRMQTIKEIHEYLSQRLR IKEEDMRLWLYNSENYLTLLDD EDHKLEYLKIQDEQHLVIEVRN KDMSWPEEMSFIANSSKIDRHK VPTEKGATGLSNLGNTCFMNSS IQCVSNTQPLTQYFISGRHLYE LNRTNPIGMKGHMAKCYGDLVQ ELWSGTQKNVAPLKLRWTIAKY APRFNGFQQQDSQELLAFLLDG LHEDLNRVHEKPYVELKDSDGR PDWEVAAEAWDNHLRRNRSIVV DLFHGQLRSQVKCKTCGHISVR FDPFNFLSLPLPMDSYMHLEIT VIKLDGTTPVRYGLRLNMDEKY TGLKKQLSDLCGLNSEQILLAE VHGSNIKNFPQDNQKVRLSVSG FLCAFEIPVPVSPISASSPTQT DFSSSPSTNEMFTLTTNGDLPR PIFIPNGMPNTVVPCGTEKNFT NGMVNGHMPSLPDSPFTGYIIA VHRKMMRTELYFLSSQKNRPSL FGMPLIVPCTVHTRKKDLYDAV WIQVSRLASPLPPQEASNHAQD CDDSMGYQYPFTLRVVQKDGNS CAWCPWYRFCRGCKIDCGEDRA FIGNAYIAVDWDPTALHLRYQT SQERVVDEHESVEQSRRAQAEP INLDSCLRAFTSEEELGENEMY YCSKCKTHCLATKKLDLWRLPP ILIIHLKRFQFVNGRWIKSQKI VKFPRESFDPSAFLVPRDPALC QHKPLTPQGDELSEPRILAREV KKVDAQSSAGEEDVLLSKSPSS LSANIISSPKGSPSSSRKSGTS CPSSKNSSPNSSPRTLGRSKGR LRLPQIGSKNKLSSSKENLDAS KENGAGQICELADALSRGHVLG GSQPELVTPQDHEVALANGFLY EHEACGNGYSNGQLGNHSEEDS TDDQREDTRIKPIYNLYAISCH SGILGGGHYVTYAKNPNCKWYC		CTVHTRKKDLYDAVWIQVSR LASPLPPQEASNHAQDCDDS MGYQYPFTLRVVQKDGNSCA WCPWYRFCRGCKIDCGEDRA FIGNAYIAVDWDPTALHLRY QTSQERVVDEHESVEQSRRA QAEPINLDSCLRAFTSEEEL GENEMYYCSKCKTHCLATKK LDLWRLPPILIIHLKRFQFV NGRWIKSQKIVKFPRESFDP SAFLVPRDPALCQHKPLTPQ GDELSEPRILAREVKKVDAQ SSAGEEDVLLSKSPSSLSAN IISSPKGSPSSSRKSGTSCP SSKNSSPNSSPRTLGRSKGR LRLPQIGSKNKLSSSKENLD ASKENGAGQICELADALSRG HVLGGSQPELVTPQDHEVAL ANGFLYEHEACGNGYSNGQL GNHSEEDSTDDQREDTRIKP IYNLYAISCHSGILGGGHYV TYAKNPNCKWYCYNDSSCKE LHPDEIDTDSAYILFYEQQG IDYAQFLPKTDGKKMADTSS MDEDFESDYKKYCVLQ

		YNDSSCKELHPDEIDTDSAYIL FYEQQGIDYAQFLPKTDGKKMA DTSSMDEDFESDYKKYCVLQ		
U17L6_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 6	17	MEDDSLYLRGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KTLTLHTSAKVLILVLKRFSDV TGNKIAKNVQYPECLDMQPYMS QQNTGPLVYVLYAVLVHAGWSC HNGHYFSYVKAQEGQWYKMDDA EVTASSITSVLSQQAYVLFYIQ KSEWERHSESVSRGREPRALGS ED	129	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQQNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS
UBP42_HUMAN Ubiquitin carboxyl-terminal hydrolase 42	18	MTIVDKASESSDPSAYQNQPGS SEAVSPGDMDAGSASWGAVSSL NDVSNHTLSLGPVPGAVVYSSS SVPDKSKPSPQKDQALGDGIAP PQKVLFPSEKICLKWQQTHRVG AGLQNLGNTCFANAALQCLTYT PPLANYMLSHEHSKTCHAEGFC MMCTMQAHITQALSNPGDVIKP MFVINEMRRIARHFRFGNQEDA HEFLQYTVDAMQKACLNGSNKL DRHTQATTLVCQIFGGYLRSRV KCLNCKGVSDTFDPYLDITLEI KAAQSVNKALEQFVKPEQLDGE NSYKCSKCKKMVPASKRFTIHR SSNVLTLSLKRFANFTGGKIAK DVKYPEYLDIRPYMSQPNGEPI VYVLYAVLVHTGFNCHAGHYFC YIKASNGLWYQMNDSIVSTSDI RSVLSQQAYVLFYIRSHDVKNG GELTHPTHSPGQSSPRPVISQR VVTNKQAAPGFIGPQLPSHMIK NPPHLNGTGPLKDTPSSSMSSP NGNSSVNRASPVNASASVQNWS VNRSSVIPEHPKKQKITISIHN KLPVRQCQSQPNLHSNSLENPT KPVPSSTITNSAVQSTSNASTM SVSSKVTKPIPRSESCSQPVMN GKSKLNSSVLVPYGAESSEDSD EESKGLGKENGIGTIVSSHSPG	130	RVGAGLQNLGNTCFANAALQ CLTYTPPLANYMLSHEHSKT CHAEGFCMMCTMQAHITQAL SNPGDVIKPMFVINEMRRIA RHFRFGNQEDAHEFLQYTVD AMQKACLNGSNKLDRHTQAT TLVCQIFGGYLRSRVKCLNC KGVSDTFDPYLDITLEIKAA QSVNKALEQFVKPEQLDGEN SYKCSKCKKMVPASKRFTIH RSSNVLTLSLKRFANFTGGK IAKDVKYPEYLDIRPYMSQP NGEPIVYVLYAVLVHTGFNC HAGHYFCYIKASNGLWYQMN DSIVSTSDIRSVLSQQAYVL FYIRSHDVKNGGE

		QDAEDEEATPHELQEPMTLNGA NSADSDSDPKENGLAPDGASCQ GQPALHSENPFAKANGLPGKLM PAPLLSLPEDKILETFRLSNKL KGSTDEMSAPGAERGPPEDRDA EPQPGSPAAESLEEPDAAAGLS STKKAPPPRDPGTPATKEGAWE AMAVAPEEPPPSAGEDIVGDTA PPDLCDPGSLTGDASPLSQDAK GMIAEGPRDSALAEAPEGLSPA PPARSEEPCEQPLLVHPSGDHA RDAQDPSQSLGAPEAAERPPAP VLDMAPAGHPEGDAEPSPGERV EDAAAPKAPGPSPAKEKIGSLR KVDRGHYRSRRERSSSGEPARE SRSKTEGHRHRRRRTCPRERDR QDRHAPEHHPGHGDRLSPGERR SLGRCSHHHSRHRSGVELDWVR HHYTEGERGWGREKFYPDRPRW DRCRYYHDRYALYAARDWKPFH GGREHERAGLHERPHKDHNRGR RGCEPARERERHRPSSPRAGAP HALAPHPDRFSHDRTALVAGDN CNLSDRFHEHENGKSRKRRHDS VENSDSHVEKKARRSEQKDPLE EPKAKKHKKSKKKKKSKDKHRD RDSRHQQDSDLSAACSDADLHR HKKKKKKKKRHSRKSEDFVKDS ELHLPRVTSLETVAQFRRAQGG FPLSGGPPLEGVGPFREKTKHL RMESRDDRCRLFEYGQGKRRYL ELGR		
U17L7_HUMAN Inactive ubiquitin carboxyl-terminal hydrolase 17-like protein 7	19	MEDDSLYLGGDWQFNHFSKLTS SRLDAAFAEIQRTSLSEKSPLS SETRFDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQKIGNT FYVNVSLQCLTYTLPLSNYMLS REDSQTCHLHKCCMFCTMQAHI TWALHSPGHVIQPSQVLAAGFH RGEQEDAHEFLMFTVDAMKKAC LPGHKQLDHHSKDTTLIHQIFG AYWRSQIKYLHCHGVSDTFDPY LDIALDIQAAQSVKQALEQLVK PKELNGENAYHCGLCLQKAPAS KTLTLPTSAKVLILVLKRFSDV TGNKLAKNVQYPKCRDMQPYMS QQNTGPLVYVLYAVLVHAGWSC HNGHYFSYVKAQEGQWYKMDDA EVTASGITSVLSQQAYVLFYIQ KSEWERHSESVSRGREPRALGA EDTDRPATQGELKRDHPCLQVP	131	AVGAGLQKIGNTFYVNVSLQ CLTYTLPLSNYMLSREDSQT CHLHKCCMFCTMQAHITWAL HSPGHVIQPSQVLAAGFHRG EQEDAHEFLMFTVDAMKKAC LPGHKQLDHHSKDTTLIHQI FGAYWRSQIKYLHCHGVSDT FDPYLDIALDIQAAQSVKQA LEQLVKPKELNGENAYHCGL CLQKAPASKTLTLPTSAKVL ILVLKRFSDVTGNKLAKNVQ YPKCRDMQPYMSQQNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SGITSVLSQQAYVLFYIQKS EWERHSESVSRGREPRALGA EDTDRPATQGELKRDHPCLQ VPEL

		ELDEHLVERATQESTLDHWKFP QEQNKTKPEFNVRKVEGTLPPN VLVIHQSKYKCGMKNHHPEQQS SLLNLSSTKPTDQESMNTGTLA SLQGSTRRSKGNNKHSKRSLLV CQ		
U17LH_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 17	20	MEDDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KTLTLHTSAKVLILVLKRFSDV TGNKIAKNVQYPECLDMQPYMS QQNTGPLVYVLYAVLVHAGWSC HNGHYFSYVKAQEGQWYKMDDA EVTAASITSVLSQQAYVLFYIQ KSEWERHSESVSRGREPRALGA EDTDRRATQGELKRDHPCLQAP ELDEHLVERATQESTLDHWKFL QEQNKTKPEFNVRKVEGTLPPD VLVIHQSKYKCGMKNHHPEQQS SLLNLSSSTPTHQESMNTGTLA SLRGRARRSKGKNKHSKRALLV CQ	132	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQQNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA ASITSVLSQQAYVLFYIQKS EWERHSESVSRGREPRALGA EDTDRRATQGELKRDHPCLQ APEL
UBP13_HUMAN Ubiquitin carboxyl-terminal hydrolase 13	21	MQRRGALFGMPGGSGGRKMAAG DIGELLVPHMPTIRVPRSGDRV YKNECAFSYDSPNSEGGLYVCM NTFLAFGREHVERHFRKTGQSV YMHLKRHVREKVRGASGGALPK RRNSKIFLDLDTDDDLNSDDYE YEDEAKLVIFPDHYEIALPNIE ELPALVTIACDAVLSSKSPYRK QDPDTWENELPVSKYANNLTQL DNGVRIPPSGWKCARCDLRENL WLNLTDGSVLCGKWFFDSSGGN GHALEHYRDMGYPLAVKLGTIT PDGADVYSFQEEEPVLDPHLAK HLAHFGIDMLHMHGTENGLQDN DIKLRVSEWEVIQESGTKLKPM YGPGYTGLKNLGNSCYLSSVMQ AIFSIPEFQRAYVGNLPRIFDY SPLDPTQDFNTQMTKLGHGLLS GQYSKPPVKSELIEQVMKEEHK PQQNGISPRMFKAFVSKSHPEF	133	YGPGYTGLKNLGNSCYLSSV MQAIFSIPEFQRAYVGNLPR IFDYSPLDPTQDFNTQMTKL GHGLLSGQYSKPPVKSELIE QVMKEEHKPQQNGISPRMFK AFVSKSHPEFSSNRQQDAQE FFLHLVNLVERNRIGSENPS DVFRFLVEERIQCCQTRKVR YTERVDYLMQLPVAMEAATN KDELIAYELTRREAEANRRP LPELVRAKIPFSACLQAFSE PENVDDFWSSALQAKSAGVK TSRFASFPEYLVVQIKKFTF GLDWVPKKFDVSIDMPDLLD INHLRARGLQPGEEELPDIS PPIVIPDDSKDRLMNQLIDP SDIDESSVMQLAEMGFPLEA CRKAVYFTGNMGAEVAFNWI IVHMEEPDFAEPLTMPGYGG AASAGASVFGASGLDNQPPE

		SSNRQQDAQEFFLHLVNLVERN RIGSENPSDVFRFLVEERIQCC QTRKVRYTERVDYLMQLPVAME AATNKDELIAYELTRREAEANR RPLPELVRAKIPFSACLQAFSE PENVDDFWSSALQAKSAGVKTS RFASFPEYLVVQIKKFTFGLDW VPKKFDVSIDMPDLLDINHLRA RGLQPGEEELPDISPPIVIPDD SKDRLMNQLIDPSDIDESSVMQ LAEMGFPLEACRKAVYFTGNMG AEVAFNWIIVHMEEPDFAEPLT MPGYGGAASAGASVFGASGLDN QPPEEIVAIITSMGFQRNQAIQ ALRATNNNLERALDWIFSHPEF EEDSDFVIEMENNANANIISEA KPEGPRVKDGSGTYELFAFISH MGTSTMSGHYICHIKKEGRWVI YNDHKVCASERPPKDLGYMYFY RRIPS		EIVAIITSMGFQRNQAIQAL RATNNNLERALDWIFSHPEF EEDSDFVIEMENNANANIIS EAKPEGPRVKDGSGTYELFA FISHMGTSTMSGHYICHIKK EGRWVIYNDHKVCASERPPK DLGYMYFYRRIPS
UBP11_HUMAN Ubiquitin carboxyl-terminal hydrolase 11	22	MAVAPRLFGGLCFRFRDQNPEV AVEGRLPISHSCVGCRRERTAM ATVAANPAAAAAAVAAAAAVTE DREPQHEELPGLDSQWRQIENG ESGRERPLRAGESWFLVEKHWY KQWEAYVQGGDQDSSTFPGCIN NATLFQDEINWRLKEGLVEGED YVLLPAAAWHYLVSWYGLEHGQ PPIERKVIELPNIQKVEVYPVE LLLVRHNDLGKSHTVQFSHTDS IGLVLRTARERFLVEPQEDTRL WAKNSEGSLDRLYDTHITVLDA ALETGQLIIMETRKKDGTWPSA QLHVMNNNMSEEDEDFKGQPGI CGLTNLGNTCFMNSALQCLSNV PQLTEYFLNNCYLEELNFRNPL GMKGEIAEAYADLVKQAWSGHH RSIVPHVFKNKVGHFASQFLGY QQHDSQELLSFLLDGLHEDLNR VKKKEYVELCDAAGRPDQEVAQ EAWQNHKRRNDSVIVDTFHGLF KSTLVCPDCGNVSVTFDPFCYL SVPLPISHKRVLEVFFIPMDPR RKPEQHRLVVPKKGKISDLCVA LSKHTGISPERMMVADVFSHRF YKLYQLEEPLSSILDRDDIFVY EVSGRIEAIEGSREDIVVPVYL RERTPARDYNNSYYGLMLFGHP LLVSVPRDRFTWEGLYNVLMYR LSRYVTKPNSDDEDDGDEKEDD EEDKDDVPGPSTGGSLRDPEPE	134	KGQPGICGLTNLGNTCFMNS ALQCLSNVPQLTEYFLNNCY LEELNFRNPLGMKGEIAEAY ADLVKQAWSGHHRSIVPHVF KNKVGHFASQFLGYQQHDSQ ELLSFLLDGLHEDLNRVKKK EYVELCDAAGRPDQEVAQEA WQNHKRRNDSVIVDTFHGLF KSTLVCPDCGNVSVTFDPFC YLSVPLPISHKRVLEVFFIP MDPRRKPEQHRLVVPKKGKI SDLCVALSKHTGISPERMMV ADVFSHRFYKLYQLEEPLSS ILDRDDIFVYEVSGRIEAIE GSREDIVVPVYLRERTPARD YNNSYYGLMLFGHPLLVSVP RDRFTWEGLYNVLMYRLSRY VTKPNSDDEDDGDEKEDDEE DKDDVPGPSTGGSLRDPEPE QAGPSSGVTNRCPFLLDNCL GTSQWPPRRRRKQLFTLQTV NSNGTSDRTTSPEEVHAQPY IAIDWEPEMKKRYYDEVEAE GYVKHDCVGYVMKKAPVRLQ ECIELFTTVETLEKENPWYC PSCKQHQLATKKLDLWMLPE ILIIHLKRFSYTKFSREKLD TLVEFPIRDLDFSEFVIQPQ NESNPELYKYDLIAVSNHYG GMRDGHYTTFACNKDSGQWH

		QAGPSSGVTNRCPFLLDNCLGT SQWPPRRRRKQLFTLQTVNSNG TSDRTTSPEEVHAQPYIAIDWE PEMKKRYYDEVEAEGYVKHDCV GYVMKKAPVRLQECIELFTTVE TLEKENPWYCPSCKQHQLATKK LDLWMLPEILIIHLKRFSYTKF SREKLDTLVEFPIRDLDFSEFV IQPQNESNPELYKYDLIAVSNH YGGMRDGHYTTFACNKDSGQWH YFDDNSVSPVNENQIESKAAYV LFYQRQDVARRLLSPAGSSGAP ASPACSSPPSSEFMDVN		YFDDNSVSPVNENQIESKAA YVLFYQRQD
U17L1_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 1	23	MGDDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS SETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYENASLQCLTYTLPLANYMLS REHSQTCQRPKCCMLCTMQAHI TWALHSPGHVIQPSQALAAGFH RGKQEDVHEFLMFTVDAMKKAC LPGHKQVDHHCKDTTLIHQIFG GCWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVKQALEQLVK PEELNGENAYHCGLCLQRAPAS NTLTLHTSAKVLILVLKRFSDV AGNKLAKNVQYPECLDMQPYMS QQNTGPLVYVLYAVLVHAGWSC HDGHYFSYVKAQEVQWYKMDDA EVTVCSIISVLSQQAYVLFYIQ KSEWERHSESVSRGREPRALGA EDTDRRAKQGELKRDHPCLQAP ELDEHLVERATQESTLDHWKFL QEQNKTKPEFNVGKVEGTLPPN ALVIHQSKYKCGMKNHHPEQQS SLLNLSSTTRTDQESMNTGTLA SLQGRTRRAKGKNKHSKRALLV CQ	135	AVGAGLQNMGNTCYENASLQ CLTYTLPLANYMLSREHSQT CQRPKCCMLCTMQAHITWAL HSPGHVIQPSQALAAGFHRG KQEDVHEFLMFTVDAMKKAC LPGHKQVDHHCKDTTLIHQI FGGCWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVKQA LEQLVKPEELNGENAYHCGL CLQRAPASNTLTLHTSAKVL ILVLKRFSDVAGNKLAKNVQ YPECLDMQPYMSQQNTGPLV YVLYAVLVHAGWSCHDGHYF SYVKAQEVQWYKMDDAEVTV CSIISVLSQQAYVLFYIQKS
UBP14_HUMAN Ubiquitin carboxyl-terminal hydrolase 14	24	MPLYSVTVKWGKEKFEGVELNT DEPPMVFKAQLFALTGVQPARQ KVMVKGGTLKDDDWGNIKIKNG MTLLMMGSADALPEEPSAKTVF VEDMTEEQLASAMELPCGLTNL GNTCYMNATVQCIRSVPELKDA LKRYAGALRASGEMASAQYITA ALRDLFDSMDKTSSSIPPIILL QFLHMAFPQFAEKGEQGQYLQQ DANECWIQMMRVLQQKLEAIED DSVKETDSSSASAATPSKKKSL IDQFFGVEFETTMKCTESEEEE VTKGKENQLQLSCFINQEVKYL	136	ASAMELPCGLTNLGNTCYMN ATVQCIRSVPELKDALKRYA GALRASGEMASAQYITAALR DLFDSMDKTSSSIPPIILLQ FLHMAFPQFAEKGEQGQYLQ QDANECWIQMMRVLQQKLEA IEDDSVKETDSSSASAATPS KKKSLIDQFFGVEFETTMKC TESEEEEVTKGKENQLQLSC FINQEVKYLFTGLKLRLQEE ITKQSPTLQRNALYIKSSKI SRLPAYLTIQMVRFFYKEKE SVNAKVLKDVKFPLMLDMYE

		FTGLKLRLQEEITKQSPTLQRN ALYIKSSKISRLPAYLTIQMVR FFYKEKESVNAKVLKDVKFPLM LDMYELCTPELQEKMVSFRSKF KDLEDKKVNQQPNTSDKKSSPQ KEVKYEPFSFADDIGSNNCGYY DLQAVLTHQGRSSSSGHYVSWV KRKQDEWIKFDDDKVSIVTPED ILRLSGGGDWHIAYVLLYGPRR VEIMEEESEQ		LCTPELQEKMVSFRSKFKDL EDKKVNQQPNTSDKKSSPQK EVKYEPFSFADDIGSNNCGY YDLQAVLTHQGRSSSSGHYV SWVKRKQDEWIKFDDDKVSI VTPEDILRLSGGGDWHIAYV LLYGPRR
Q13107|UBP4_HUMAN Ubiquitin carboxyl-terminal hydrolase 4	25	MAEGGGCRERPDAETQKSELGP LMRTTLQRGAQWYLIDSRWFKQ WKKYVGFDSWDMYNVGEHNLFP GPIDNSGLFSDPESQTLKEHLI DELDYVLVPTEAWNKLLNWYGC VEGQQPIVRKVVEHGLFVKHCK VEVYLLELKLCENSDPTNVLSC HFSKADTIATIEKEMRKLFNIP AERETRLWNKYMSNTYEQLSKL DNTVQDAGLYQGQVLVIEPQNE DGTWPRQTLQSKSSTAPSRNFT TSPKSSASPYSSVSASLIANGD STSTCGMHSSGVSRGGSGFSAS YNCQEPPSSHIQPGLCGLGNLG NTCFMNSALQCLSNTAPLTDYF LKDEYEAEINRDNPLGMKGEIA EAYAELIKQMWSGRDAHVAPRM FKTQVGRFAPQFSGYQQQDSQE LLAFLLDGLHEDLNRVKKKPYL ELKDANGRPDAVVAKEAWENHR LRNDSVIVDTFHGLFKSTLVCP ECAKVSVTFDPFCYLTLPLPLK KDRVMEVFLVPADPHCRPTQYR VTVPLMGAVSDLCEALSRLSGI AAENMVVADVYNHRFHKIFQMD EGLNHIMPRDDIFVYEVCSTSV DGSECVTLPVYFRERKSRPSST SSASALYGQPLLLSVPKHKLTL ESLYQAVCDRISRYVKQPLPDE FGSSPLEPGACNGSRNSCEGED EEEMEHQEEGKEQLSETEGSGE DEPGNDPSETTQKKIKGQPCPK RLFTFSLVNSYGTADINSLAAD GKLLKLNSRSTLAMDWDSETRR LYYDEQESEAYEKHVSMLQPQK KKKTTVALRDCIELFTTMETLG EHDPWYCPNCKKHQQATKKFDL WSLPKILVVHLKRFSYNRYWRD KLDTVVEFPIRGLNMSEFVCNL SARPYVYDLIAVSNHYGAMGVG HYTAYAKNKLNGKWYYFDDSNV	137	SHIQPGLCGLGNLGNTCFMN SALQCLSNTAPLTDYFLKDE YEAEINRDNPLGMKGEIAEA YAELIKQMWSGRDAHVAPRM FKTQVGRFAPQFSGYQQQDS QELLAFLLDGLHEDLNRVKK KPYLELKDANGRPDAVVAKE AWENHRLRNDSVIVDTFHGL FKSTLVCPECAKVSVTFDPF CYLTLPLPLKKDRVMEVFLV PADPHCRPTQYRVTVPLMGA VSDLCEALSRLSGIAAENMV VADVYNHRFHKIFQMDEGLN HIMPRDDIFVYEVCSTSVDG SECVTLPVYFRERKSRPSST SSASALYGQPLLLSVPKHKL TLESLYQAVCDRISRYVKQP LPDEFGSSPLEPGACNGSRN SCEGEDEEEMEHQEEGKEQL SETEGSGEDEPGNDPSETTQ KKIKGQPCPKRLFTFSLVNS YGTADINSLAADGKLLKLNS RSTLAMDWDSETRRLYYDEQ ESEAYEKHVSMLQPQKKKKT TVALRDCIELFTTMETLGEH DPWYCPNCKKHQQATKKFDL WSLPKILVVHLKRFSYNRYW RDKLDTVVEFPIRGLNMSEF VCNLSARPYVYDLIAVSNHY GAMGVGHYTAYAKNKLNGKW YYFDDSNVSLASEDQIVTKA AYVLFYQRRD

		SLASEDQIVTKAAYVLFYQRRD DEFYKTPSLSSSGSSDGGTRPS SSQQGFGDDEACSMDTN		
UBP26_HUMAN Ubiquitin carboxyl-terminal hydrolase 26	26	MAALFLRGFVQIGNCKTGISKS KEAFIEAVERKKKDRLVLYFKS GKYSTFRLSDNIQNVVLKSYRG NQNHLHLTLQNNNGLFIEGLSS TDAEQLKIFLDRVHQNEVQPPV RPGKGGSVFSSTTQKEINKTSF HKVDEKSSSKSFEIAKGSGTGV LQRMPLLTSKLTLTCGELSENQ HKKRKRMLSSSSEMNEEFLKEN NSVEYKKSKADCSRCVSYNREK QLKLKELEENKKLECESSCIMN ATGNPYLDDIGLLQALTEKMVL VFLLQQGYSDGYTKWDKLKLFF ELFPEKICHGLPNLGNTCYMNA VLQSLLSIPSFADDLLNQSFPW GKIPLNALTMCLARLLFFKDTY NIEIKEMLLLNLKKAISAAAEI FHGNAQNDAHEFLAHCLDQLKD NMEKLNTIWKPKSEFGEDNFPK QVFADDPDTSGFSCPVITNFEL ELLHSIACKACGQVILKTELNN YLSINLPQRIKAHPSSIQSTFD LFFGAEELEYKCAKCEHKTSVG VHSFSRLPRILIVHLKRYSLNE FCALKKNDQEVIISKYLKVSSH CNEGTRPPLPLSEDGEITDFQL LKVIRKMTSGNISVSWPATKES KDILAPHIGSDKESEQKKGQTV FKGASRRQQQKYLGKNSKPNEL ESVYSGDRAFIEKEPLAHLMTY LEDTSLCQFHKAGGKPASSPGT PLSKVDFQTVPENPKRKKYVKT SKFVAFDRIINPTKDLYEDKNI RIPERFQKVSEQTQQCDGMRIC EQAPQQALPQSFPKPGTQGHTK NLLRPTKLNLQKSNRNSLLALG SNKNPRNKDILDKIKSKAKETK RNDDKGDHTYRLISVVSHLGKT LKSGHYICDAYDFEKQIWFTYD DMRVLGIQEAQMQEDRRCTGYI FFYMHNEIFEEMLKREENAQLN SKEVEETLQKE	138	KICHGLPNLGNTCYMNAVLQ SLLSIPSFADDLLNQSFPWG KIPLNALTMCLARLLFFKDT YNIEIKEMLLLNLKKAISAA AEIFHGNAQNDAHEFLAHCL DQLKDNMEKLNTIWKPKSEF GEDNFPKQVFADDPDTSGFS CPVITNFELELLHSIACKAC GQVILKTELNNYLSINLPQR IKAHPSSIQSTFDLFFGAEE LEYKCAKCEHKTSVGVHSFS RLPRILIVHLKRYSLNEFCA LKKNDQEVIISKYLKVSSHC NEGTRPPLPLSEDGEITDFQ LLKVIRKMTSGNISVSWPAT KESKDILAPHIGSDKESEQK KGQTVFKGASRRQQQKYLGK NSKPNELESVYSGDRAFIEK EPLAHLMTYLEDTSLCQFHK AGGKPASSPGTPLSKVDFQT VPENPKRKKYVKTSKFVAFD RIINPTKDLYEDKNIRIPER FQKVSEQTQQCDGMRICEQA PQQALPQSFPKPGTQGHTKN LLRPTKLNLQKSNRNSLLAL GSNKNPRNKDILDKIKSKAK ETKRNDDKGDHTYRLISVVS HLGKTLKSGHYICDAYDFEK QIWFTYDDMRVLGIQEAQMQ EDRRCTGYIFFYMHN
UBP19_HUMAN Ubiquitin carboxyl-terminal hydrolase 19	27	MSGGASATGPRRGPPGLEDTTS KKKQKDRANQESKDGDPRKETG SRYVAQAGLEPLASGDPSASAS HAAGITGSRHRTRLFFPSSSGS ASTPQEEQTKEGACEDPHDLLA TPTPELLLDWRQSAEEVIVKLR	139	LPGFTGLVNLGNTCFMNSVI QSLSNTRELRDFFHDRSFEA EINYNNPLGTGGRLAIGFAV LLRALWKGTHHAFQPSKLKA IVASKASQFTGYAQHDAQEF MAFLLDGLHEDLNRIQNKPY

		VGVGPLQLEDVDAAFTDTDCVV RFAGGQQWGGVFYAEIKSSCAK VQTRKGSLLHLTLPKKVPMLTW PSLLVEADEQLCIPPLNSQTCL LGSEENLAPLAGEKAVPPGNDP VSPAMVRSRNPGKDDCAKEEMA VAADAATLVDEPESMVNLAFVK NDSYEKGPDSVVVHVYVKEICR DTSRVLFREQDFTLIFQTRDGN FLRLHPGCGPHTTFRWQVKLRN LIEPEQCTFCFTASRIDICLRK RQSQRWGGLEAPAARVGGAKVA VPTGPTPLDSTPPGGAPHPLTG QEEARAVEKDKSKARSEDTGLD SVATRTPMEHVTPKPETHLASP KPTCMVPPMPHSPVSGDSVEEE EEEEKKVCLPGFTGLVNLGNTC FMNSVIQSLSNTRELRDFFHDR SFEAEINYNNPLGTGGRLAIGF AVLLRALWKGTHHAFQPSKLKA IVASKASQFTGYAQHDAQEFMA FLLDGLHEDLNRIQNKPYTETV DSDGRPDEVVAEEAWQRHKMRN DSFIVDLFQGQYKSKLVCPVCA KVSITFDPFLYLPVPLPQKQKV LPVFYFAREPHSKPIKFLVSVS KENSTASEVLDSLSQSVHVKPE NLRLAEVIKNRFHRVFLPSHSL DTVSPSDTLLCFELLSSELAKE RVVVLEVQQRPQVPSVPISKCA ACQRKQQSEDEKLKRCTRCYRV GYCNQLCQKTHWPDHKGLCRPE NIGYPFLVSVPASRLTYARLAQ LLEGYARYSVSVFQPPFQPGRM ALESQSPGCTTLLSTGSLEAGD SERDPIQPPELQLVTPMAEGDT GLPRVWAAPDRGPVPSTSGISS EMLASGPIEVGSLPAGERVSRP EAAVPGYQHPSEAMNAHTPQFF IYKIDSSNREQRLEDKGDTPLE LGDDCSLALVWRNNERLQEFVL VASKELECAEDPGSAGEAARAG HFTLDQCLNLFTRPEVLAPEEA WYCPQCKQHREASKQLLLWRLP NVLIVQLKRFSFRSFIWRDKIN DLVEFPVRNLDLSKFCIGQKEE QLPSYDLYAVINHYGGMIGGHY TACARLPNDRSSQRSDVGWRLF DDSTVTTVDESQVVTRYAYVLF YRRRNSPVERPPRAGHSEHHPD LGPAAEAAASQASRIWQELEAE		TETVDSDGRPDEVVAEEAWQ RHKMRNDSFIVDLFQGQYKS KLVCPVCAKVSITFDPFLYL PVPLPQKQKVLPVFYFAREP HSKPIKFLVSVSKENSTASE VLDSLSQSVHVKPENLRLAE VIKNRFHRVFLPSHSLDTVS PSDTLLCFELLSSELAKERV VVLEVQQRPQVPSVPISKCA ACQRKQQSEDEKLKRCTRCY RVGYCNQLCQKTHWPDHKGL CRPENIGYPFLVSVPASRLT YARLAQLLEGYARYSVSVFQ PPFQPGRMALESQSPGCTTL LSTGSLEAGDSERDPIQPPE LQLVTPMAEGDTGLPRVWAA PDRGPVPSTSGISSEMLASG PIEVGSLPAGERVSRPEAAV PGYQHPSEAMNAHTPQFFIY KIDSSNREQRLEDKGDTPLE LGDDCSLA LVWRNNERLQEFVLVASKEL ECAEDPGSAGEAARAGHFTL DQCLNLFTRPEVLAPEEAWY CPQCKQHREASKQLLLWRLP NVLIVQLKRFSFRSFIWRDK INDLVEFPVRNLDLSKFCIG QKEEQLPSYDLYAVINHYGG MIGGHYTACARLPNDRSSQR SDVGWRLFDDSTVTTVDESQ VVTRYAYVLFYRRRN

		EEPVPEGSGPLGPWGPQDWVGP LPRGPTTPDEGCLRYFVLGTVA ALVALVLNVFYPLVSQSRWR		
UBP10_HUMAN Ubiquitin carboxyl-terminal hydrolase 10	28	MALHSPQYIFGDFSPDEFNQFF VTPRSSVELPPYSGTVLCGTQA VDKLPDGQEYQRIEFGVDEVIE PSDTLPRTPSYSISSTLNPQAP EFILGCTASKITPDGITKEASY GSIDCQYPGSALALDGSSNVEA EVLENDGVSGGLGQRERKKKKK RPPGYYSYLKDGGDDSISTEAL VNGHANSAVPNSVSAEDAEFMG DMPPSVTPRTCNSPQNSTDSVS DIVPDSPFPGALGSDTRTAGQP EGGPGADFGQSCFPAEAGRDTL SRTAGAQPCVGTDTTENLGVAN GQILESSGEGTATN GVELHTTESIDLDPTKPESASP PADGTGSASGTLPVSQPKSWAS LFHDSKPSSSSPVAYVETKYSP PAISPLVSEKQVEVKEGLVPVS EDPVAIKIAELLENVTLIHKPV SLQPRGLINKGNWCYINATLQA LVACPPMYHLMKFIPLYSKVQR PCTSTPMIDSFVRLMNEFTNMP VPPKPRQALGDKIVRDIRPGAA FEPTYIYRLLTVNKSSLSEKGR QEDAEEYLGFILNGLHEEMLNL KKLLSPSNEKLTISNGPKNHSV NEEEQEEQGEGSEDEWEQVGPR NKTSVTRQADFVQT PITGIFGGHIRSVVYQQSSKES ATLQPFFTLQLDIQSDKIRTVQ DALESLVARESVQGYTTKTKQE VEISRRVTLEKLPPVLVLHLKR FVYEKTGGCQKLIKNIEYPVDL EISKELLSPGVKNKNFKCHRTY RLFAVVYHHGNSATGGHYTTDV FQIGLNGWLRIDDQTVKVINQY QVVKPTAERTAYLLYYRRVDLL	140	SLQPRGLINKGNWCYINATL QALVACPPMYHLMKFIPLYS KVQRPCTSTPMIDSFVRLMN EFTNMPVPPKPRQALGDKIV RDIRPGAAFEPTYIYRLLTV NKSSLSEKGRQEDAEEYLGF ILNGLHEEMLNLKKLLSPSN EKLTISNGPKNHSVNEEEQE EQGEGSEDEWEQVGPRNKTS VTRQADFVQTPITGIFGGHI RSVVYQQSSKESATLQPFFT LQLDIQSDKIRTVQDALESL VARESVQGYTTKTKQEVEIS RRVTLEKLPPVLVLHLKRFV YEKTGGCQKLIKNIEYPVDL EISKELLSPGVKNKNFKCHR TYRLFAVVYHHGNSATGGHY TTDVFQIGLNGWLRIDDQTV KVINQYQVVKPTAERTAYLL YYRRVD
UBP49_HUMAN Ubiquitin carboxyl-terminal hydrolase 49	29	MDRCKHVGRLRLAQDHSILNPQ KWCCLECATTESVWACLKCSHV ACGRYIEDHALKHFEETGHPLA MEVRDLYVFCYLCKDYVLNDNP EGDLKLLRSSLLAVRGQKQDTP VRRGRTLRSMASGEDVVLPQRA PQGQPQMLTALWYRRQRLLART LRLWFEKSSRGQAKLEQRRQEE ALERKKEEARRRRREVKRRLLE ELASTPPRKSARLLLHTPRDAG PAASRPAALPTSRRVPAATLKL	141	MDRCKHVGRLRLAQDHSILN PQKWCCLECATTESVWACLK CSHVACGRYIEDHALKHFEE TGHPLAMEVRDLYVFCYLCK DYVLNDNPEGDLKLLRSSLL AVRGQKQDTPVRRGRTLRSM ASGEDVVLPQRAPQGQPQML TALWYRRQRLLARTLRLWFE KSSRGQAKLEQRRQEEALER KKEEARRRRREVKRRLLEEL ASTPPRKSARLLLHTPRDAG

		RRQPAMAPGVTGLRNLGNTCYM NSILQVLSHLQKFRECFLNLDP SKTEHLFPKATNGK TQLSGKPTNSSATELSLRNDRA EACEREGFCWNGRASISRSLEL IQNKEPSSKHISLCRELHTLFR VMWSGKWALVSPFAMLHSVWSL IPAFRGYDQQDAQEFLCELLHK VQQELESEGTTRRILIPFSQRK LTKQVLKVVNTIFHGQLLSQVT CISCNYKSNTIEPFWDLSLEFP ERYHCIEKGFVPLNQTECLLTE MLAKFTETEALEGRIYACDQCN SKRRKSNPKPLVLSEARKQLMI YRLPQVLRLHLKRFRWSGRNHR EKIGVHVVFDQVLTMEPYCCRD MLSSLDKETFAYDL SAVVMHHGKGFGSGHYTAYCYN TEGGFWVHCNDSKLNVCSVEEV CKTQAYILFYTQRTVQGNARIS ETHLQAQVQSSNNDEGRPQTFS		PAASRPAALPTSRRVPAATL KLRRQPAMAPGVTGLRNLGN TCYMNSILQVLSHLQKFREC FLNLDPSKTEHLFPKATNGK TQLSGKPTNSSATELSLRND RAEACEREGFCWNGRASISR SLELIQNKEPSSKHISLCRE LHTLFRVMWSGKWALVSPFA MLHSVWSLIPAFRGYDQQDA QEFLCELLHKVQQELESEGT TRRILIPFSQRKLTKQVLKV VNTIFHGQLLSQVTCISCNY KSNTIEPFWDLSLEFPERYH CIEKGFVPLNQTECLLTEML AKFTETEALEGRIYACDQCN SKRRKSNPKPLVLSEARKQL MIYRLPQVLRLHLKRFRWSG RNHREKIGVHVVFDQVLTME PYCCRDMLSSLDKETFAYDL SAVVMHHGKGFGSGHYTAYC YNTEGGFWVHCNDSKLNVCS VEEVCKTQAYILFYTQRT
U17L8_HUMAN Inactive ubiquitin carboxyl-terminal hydrolase 17-like protein 8	30	MEDDSLYLGGEWQFNHFSKLTS PRPDAAFAEIQRTSLPEKSPLS SETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYLNASLQCLTYTPPLANYMLS REHSQTCQRPKCCMLCTMQAHI TWALHSPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GCWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVKQALEQLVK PEELNGENAYPCGLCLQRAPAS NTLTLHTSAKVLILVLKRFCDV TGNKLAKNVQYPEC LDMQPYMSQQNTGPLVYVLYAV LVHAGWSCHNGYYFSYVKAQEG QWYKMDDAEVTACSITSVLSQQ AYVLFYIQKSEWERHSESVSRG REPRALGAEDTDRPATQGELKR DHPCLQVPELDEHLVERATEES TLDHWKFPQEQNKMKPEFNVRK VEGTLPPNVLVIHQSKYKCGMK NHHPEQQSSLLNLSSMNSTDQE SMNTGTLASLQGRTRRSKGKNK HSKRSLLVCQ	142	AVGAGLQNMGNTCYLNASLQ CLTYTPPLANYMLSREHSQT CQRPKCCMLCTMQAHITWAL HSPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGCWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVKQA LEQLVKPEELNGENAYPCGL CLQRAPASNTLTLHTSAKVL ILVLKRFCDVTGNKLAKNVQ YPECLDMQPYMSQQNTGPLV YVLYAVLVHAGWSCHNGYYF SYVKAQEGQWYKMDDAEVTA CSITSVLSQQAYVLFYIQKS
6VN6_1	31	GSKKHTGYVGLKNQGATCYMNS LLQTLFFTNQLRKAVYMMPTEG DDSSKSVPLALQRVFYELQHSD KPVGTKKLTKSFGWETLDSFMQ	143	TGYVGLKNQGATCYMNSLLQ TLFFTNQLRKAVYMMPTEGD DSSKSVPLALQRVFYELQHS DKPVGTKKLTKSFGWETLDS

		HDVQELCRVLLDNVENKMKGTC VEGTIPKLFRGKMVSYIQCKEV DYRSDRREDYYDIQLSIKGKKN IFESFVDYVAVEQLDGDNKYDA GEHGLQEAEKGVKFLTLPPVLH LQLMRFMYDPQTDQNIKINDRF EFPEQLPLDEFLQKTDPKDPAN YILHAVLVHSGDNHGGHYVVYL NPKGDGKWCKFDDDVVSRCTKE EAIEHNYGGHDDDLSVRHCTNA YMLVYIRESKLSEVLQAVTDHD IPQQLVERLQEEKRIEAQKR		FMQHDVQELCRVLLDNVENK MKGTCVEGTIPKLFRGKMVS YIQCKEVDYRSDRREDYYDI QLSIKGKKNIFESFVDYVAV EQLDGDNKYDAGEHGLQEAE KGVKFLTLPPVLHLQLMRFM YDPQTDQNIKINDRFEFPEQ LPLDEFLQKTDPKDPANYIL HAVLVHSGDNHGGHYVVYLN PKGDGKWCKFDDDVVSRCTK EEAIEHNYGGHDDDLSVRHC TNAYMLVYIRE
6DGF_1	32	AQGLAGLRNLGNTCFMNSILQC LSNTRELRDYCLQRLYMRDLHH GSNAHTALVEEFAKLIQTIWTS SPNDVVSPSEFKTQIQRYAPRF VGYNQQDAQEFLRFLLDGLHNE VNRVTLRPKSNPENLDHLPDDE KGRQMWRKYLEREDSRIGDLFV GQLKSSLTCTDCGYCSTVFDPF WDLSLPIAKRGYPEVTLMDCMR LFTKEDVLDGDEKPTCCRCRGR KRCIKKFSIQRFPKILVLHLKR FSESRIRTSKLTTFVNFPLRDL DLREFASENTNHAVYNLYAVSN HSGTTMGGHYTAYCRSPGTGEW HTFNDSSVTPMSSSQVRTSDAY LLFYELASPPSRM	144	AQGLAGLRNLGNTCFMNSIL QCLSNTRELRDYCLQRLYMR DLHHGSNAHTALVEEFAKLI QTIWTSSPNDVVSPSEFKTQ IQRYAPRFVGYNQQDAQEFL RFLLDGLHNEVNRVTLRPKS NPENLDHLPDDEKGRQMWRK YLEREDSRIGDLFVGQLKSS LTCTDCGYCSTVFDPFWDLS LPIAKRGYPEVTLMDCMRLF TKEDVLDGDEKPTCCRCRGR KRCIKKFSIQRFPKILVLHL KRFSESRIRTSKLTTFVNFP LRDLDLREFASENTNHAVYN LYAVSNHSGTTMGGHYTAYC RSPGTGEWHTFNDSSVTPMS SSQVRTSDAYLLFYELAS
2VHF_1	33	GLEIMIGKKKGIQGHYNSCYLD STLFCLFAFSSVLDTVLLRPKE KNDVEYYSETQELLRTEIVNPL RIYGYVCATKIMKLRKILEKVE AASGFTSEEKDPEEFLNILFHH ILRVEPLLKIRSAGQKVQDCYF YQIFMEKNEKVGVPTIQQLLEW SFINSNLKFAEAPSCLIIQMPR FGKDFKLFKKIFPSLELNITDL LEDTPRQCRICGGLAMYECREC YDDPDISAGKIKQFCKTCNTQV HLHPKRLNHKYNPVSLPKDLPD WDWRHGCIPCQNMELFAVLCIE TSHYVAFVKYGKDDSAWLFFDS MADRDGGQNGFNIPQVTPCPEV GEYLKMSLEDLHSLDSRRIQGC ARRLLCDAYMCMYQSPTMSLYK	145	MIGKKKGIQGHYNSCYLDST LFCLFAFSSVLDTVLLRPKE KNDVEYYSETQELLRTEIVN PLRIYGYVCATKIMKLRKIL EKVEAASGFTSEEKDPEEFL NILFHHILRVEPLLKIRSAG QKVQDCYFYQIFMEKNEKVG VPTIQQLLEWSFINSNLKFA EAPSCLIIQMPRFGKDFKLF KKIFPSLELNITDLLEDTPR QCRICGGLAMYECRECYDDP DISAGKIKQFCKTCNTQVHL HPKRLNHKYNPVSLPKDLPD WDWRHGCIPCQNMELFAVLC IETSHYVAFVKYGKDDSAWL FFDSMADRDGGQNGFNIPQV TPCPEVGEYLKMSLEDLHSL DSRRIQGCARRLLCDAYMCM YQS
U17LI_HUMAN Ubiquitin carboxyl-	34	MEDDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE	146	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL

terminal hydrolase 17-like protein 18		KLPLSSRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KTLTLHTSAKVLILVLKRFSDV TGNKIAKNVQYPEC LDMQPYMSQTNTGPLVYVLYAV LVHAGWSCHNGHYFSYVKAQEG QWYKMDDAEVTASSITSVLSQQ AYVLFYIQKSEWERHSESVSRG REPRALGAEDTDRRAKQGELKR DHPCLQAPELDEHLVERATQES TLDHWKFLQEQNKTKPEFNVRK VEGTLPPDVLVIHQSKYKCGMK NHHPEQQSSLLNLSSTTPTHQE SMNTGTLASLRGRARRSKGKNK HSKRALLVCQ		HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQTNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS
UBP22_HUMAN Ubiquitin carboxyl-terminal hydrolase 22	35	MVSRPEPEGEAMDAELAVAPPG CSHLGSFKVDNWKQNLRAIYQC FVWSGTAEARKRKAKSCICHVC GVHLNRLHSCLYCVFFGCFTKK HIHEHAKAKRHNLAIDLMYGGI YCFLCQDYIYDKDMEIIAKEEQ RKAWKMQGVGEKFSTWEPTKRE LELLKHNPKRRKITSNCTIGLR GLINLGNTCFMNCIVQALTHTP LLRDFFLSDRHRCEMQSPSSCL VCEMSSLFQEFYSGHRSPHIPY KLLHLVWTHARHLAGYEQQDAH EFLIAALDVLHRHCKGDDNGKK ANNPNHCNCIIDQIFTGGLQSD VTCQVCHGVSTTIDPFWDISLD LPGSSTPFWPLSPGSEGNVVNG ESHVSGTTTLTDCLRRFTRPEH LGSSAKIKCSGCHSYQESTKQL TMKKLPIVACFHLKRFEHSAKL RRKITTYVSFPLELDMTPFMAS SKESRMNGQYQQPTDSLNNDNK YSLFAVVNHQGTLESGHYTSFI RQHKDQWFKCDDAIITKASIKD VLDSEGYLLFYHKQFLEYE	147	LGNTCFMNCIVQALTHTPLL RDFFLSDRHRCEMQSPSSCL VCEMSSLFQEFYSGHRSPHI PYKLLHLVWTHARHLAGYEQ QDAHEFLIAALDVLHRHCKG DDNGKKANNPNHCNCIIDQI FTGGLQSDVTCQVCHGVSTT IDPFWDISLDLPGSSTPFWP LSPGSEGNVVNGESHVSGTT TLTDCLRRFTRPEHLGSSAK IKCSGCHSYQESTKQLTMKK LPIVACFHLKRFEHSAKLRR KITTYVSFPLELDMTPFMAS SKESRMNGQYQQPTDSLNND NKYSLFAVVNHQGTLESGHY TSFIRQHKDQWFKCDDAIIT KASIKDVLDSEGYLLFYHKQ F
UBP18_HUMAN Ubl carboxyl-terminal hydrolase 18	36	MSKAFGLLRQICQSILAESSQS PADLEEKKEEDSNMKREQPRER PRAWDYPHGLVGLHNIGQTCCL NSLIQVFVMNVDFTRILKRITV PRGADEQRRSVPFQMLLLLEKM	148	KGLVPGLVNLGNTCFMNSLL QGLSACPAFIRWLEEFTSQY SRDQKEPPSHQYLSLTLLHL LKALSCQEVTDDEVLDASCL LDVLRMYRWQISSFEEQDAH

		QDSRQKAVRPLELAYCLQKCNV PLFVQHDAAQLYLKLWNLIKDQ ITDVHLVERLQALYTIRVKDSL ICVDCAMESSRNSSMLTLPLSL FDVDSKPLKTLEDALHCFFQPR ELSSKSKCFCENCGKKTRGKQV LKLTHLPQTLTIHLMRFSIRNS QTRKICHSLYFPQSLDFSQILP MKRESCDAEEQSGG QYELFAVIAHVGMADSGHYCVY IRNAVDGKWFCFNDSNICLVSW EDIQCTYGNPNYHWQETAYLLV YMKMEC		ELFHVITSSLEDERDRQPRV THLFDVHSLEQQSEITPKQI TCRTRGSPHPTSNHWKSQHP FHGRLTSNMVCKHCEHQSPV RFDTFDSLSLSIPAATWGHP LTLDHCLHHFISSESVRDVV CDNCTKIEAKGTLNGEKVEH QRTTFVKQLKLGKLPQCLCI HLQRLSWSSHGTPLKRHEHV QFNEFLMMDIYKYHLLGHKP SQHNPKLNKNPGPTLELQDG PGAPTPVLNQPGAPKTQIFM NGACSPSLLPTLSAPMPFPL PVVPDYSSSTYLFRLMAVVV HHGDMHSGHFVTYRRSPPSA RNPLSTSNQWLWVSDDTVRK ASLQEVLSSSAYLLFYERVL
UBP28_HUMAN Ubiquitin carboxyl-terminal hydrolase 28	37	MTAELQQDDAAGAADGHGSSCQ MLLNQLREITGIQDPSFLHEAL KASNGDITQAVSLLTDERVKEP SQDTVATEPSEVEGSAANKEVL AKVIDLTHDNKDDLQAAIALSL LESPKIQADGRDLNRMHEATSA ETKRSKRKRCEVWGENPNPNDW RRVDGWPVGLKNVGNTCWFSAV IQSLFQLPEFRRLVLSYSLPQN VLENCRSHTEKRNIMFMQELQY LFALMMGSNRKFVDPSAALDLL KGAFRSSEEQQQDVSEFTHKLL DWLEDAFQLAVNVNSPRNKSEN PMVQLFYGTFLTEG VREGKPFCNNETFGQYPLQVNG YRNLDECLEGAMVEGDVELLPS DHSVKYGQERWFTKLPPVLTFE LSRFEFNQSLGQPEKIHNKLEF PQIIYMDRYMYRSKELIRNKRE CIRKLKEEIKILQQKLERYVKY GSGPARFPLPDMLKYVIEFAST KPASESCPPESDTHMTLPLSSV HCSVSDQTSKESTSTESSSQDV ESTFSSPEDSLPKSKPLTSSRS SMEMPSQPAPRTVTDEEINFVK TCLQRWRSEIEQDIQDLKTCIA STTQTIEQMYCDPLLRQVPYRL HAVLVHEGQANAGHYWAYIYNQ PRQSWLKYNDISVTESSWEEVE RDSYGGLRNVSAYCLMYINDKL PYFNAEAAPTESDQMSEVEALS VELKHYIQEDNWRFEQEVEEWE EEQSCKIPQMESSTNSSSQDYS TSQEPSVASSHGVRCLSSEHAV	149	GWPVGLKNVGNTCWFSAVIQ SLFQLPEFRRLVLSYSLPQN VLENCRSHTEKRNIMFMQEL QYLFALMMGSNRKFVDPSAA LDLLKGAFRSSEEQQQDVSE FTHKLLDWLEDAFQLAVNVN SPRNKSENPMVQLFYGTFLT EGVREGKPFCNNETFGQYPL QVNGYRNLDECLEGAMVEGD VELLPSDHSVKYGQERWFTK LPPVLTFELSRFEFNQSLGQ PEKIHNKLEFPQIIYMDRYM YRSKELIRNKRECIRKLKEE IKILQQKLERYVKYGSGPAR FPLPDMLKYVIEFASTKPAS ESCPPESDTHMTLPLSSVHC SVSDQTSKESTSTESSSQDV ESTFSSPEDSLPKSKPLTSS RSSMEMPSQPAPRTVTDEEI NFVKTCLQRWRSEIEQDIQD LKTCIASTTQTIEQMYCDPL LRQVPYRLHAVLVHEGQANA GHYWAYIYNQPRQSWLKYND ISVTESSWEEVERDSYGGLR NVSAYCLMYINDKLPY

		IVKEQTAQAIANTARAYEKSGV EAALSEVMLSPAMQGVILAIAK ARQTFDRDGSEAGLIKAFHEEY SRLYQLAKETPTSHSDPRLQHV LVYFFQNEAPKRVVERTLLEQF ADKNLSYDERSISIMKVAQAKL KEIGPDDMNMEEYKKWHEDYSL FRKVSVYLLTGLELYQKGKYQE ALSYLVYAYQSNAALLMKGPRR GVKESVIALYRRKCLLELNAKA ASLFETNDDHSVTEGINVMNEL IIPCIHLIINNDISKDDLDAIE VMRNHWCSYLGQDIAENLQLCL GEFLPRLLDPSAEIIVLKEPPT IRPNSPYDLCSRFAAVMESIQG VSTVTVK		
U17L2_HUMAN Ubiquitin carboxyl-terminal hydrolase 17	38	MEDDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS SEARVDLCDDLAPVARQLAPRK KLPLSSRRPAAVGAGLQNMGNT CYENASLQCLTYTPPLANYMLS REHSQTCQRPKCCMLCTMQAHI TWALHSPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GCWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVKQALEQLVK PEELNGENAYHCGLCLQRAPAS KTLTLHTSAKVLILVLKRFSDV TGNKLAKNVQYPEC LDMQPYMSQQNTGPLVYVLYAV LVHAGWSCHDGHYFSYVKAQEG QWYKMDDAKVTACSITSVLSQQ AYVLFYIQKSEWERHSESVSRG REPRALGAEDTDRRATQGELKR DHPCLQAPELDERLVERATQES TLDHWKFPQEQNKTKPEFNVRK VEGTLPPNVLVIHQSKYKCGMK NHHPEQQSSLLNLSSTTRTDQE SVNTGTLASLQGRTRRSKGKNK HSKRALLVCQ	150	AVGAGLQNMGNTCYENASLQ CLTYTPPLANYMLSREHSQT CQRPKCCMLCTMQAHITWAL HSPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGCWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVKQA LEQLVKPEELNGENAYHCGL CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKLAKNVQ YPECLDMQPYMSQQNTGPLV YVLYAVLVHAGWSCHDGHYF SYVKAQEGQWYKMDDAKVTA CSITSVLSQQAYVLFYIQKS
UBP31_HUMAN Ubiquitin carboxyl-terminal hydrolase 31	39	MSKVTAPGSGPPAAASGKEKRS FSKRLFRSGRAGGGGAGGPGAS GPAAPSSPSSPSSARSVGSFMS RVLKTLSTLSHLSSEGAAPDRG GLRSCFPPGPAAAPTPPPCPPP PASPAPPACAAEPVPGVAGLRN HGNTCFMNATLQCLSNTELFAE YLALGQYRAGRPEPSPDPEQPA GRGAQGQGEVTEQLAHLVRALW TLEYTPQHSRDFKTIVSKNALQ	151	PVPGVAGLRNHGNTCFMNAT LQCLSNTELFAEYLALGQYR AGRPEPSPDPEQPAGRGAQG QGEVTEQLAHLVRALWTLEY TPQHSRDFKTIVSKNALQYR GNSQHDAQEFLLWLLDRVHE DLNHSVKQSGQPPLKPPSET DMMPEGPSFPVCSTFVQELF QAQYRSSLTCPHCQKQSNTF DPFLCISLPIPLPHTRPLYV

		YRGNSQHDAQEFLLWLLDRVHE DLNHSVKQSGQPPLKPPSETDM MPEGPSFPVCSTFVQELFQAQY RSSLTCPHCQKQSN TFDPFLCISLPIPLPHTRPLYV TVVYQGKCSHCMRIGVAVPLSG TVARLREAVSMETKIPTDQIVL TEMYYDGFHRSFCDTDDLETVH ESDCIFAFETPEIFRPEGILSQ RGIHLNNNLNHLKFGLDYHRLS SPTQTAAKQGKMDSPTSRAGSD KIVLLVCNRACTGQQGKRFGLP FVLHLEKTIAWDLLQKEILEKM KYFLRPTVCIQVCPFSLRVVSV VGITYLLPQEEQPLCHPIVERA LKSCGPGGTAHVKLVVEWDKET RDFLFVNTEDEYIPDAESVRLQ RERHHQPQTCTLSQ CFQLYTKEERLAPDDAWRCPHC KQLQQGSITLSLWTLPDVLIIH LKRFRQEGDRRMKLQNMVKFPL TGLDMTPHVVKRSQSSWSLPSH WSPWRRPYGLGRDPEDYIYDLY AVCNHHGTMQGGHYTAYCKNSV DGLWYCFDDSDVQQLSEDEVCT QTAYILFYQRRTAIPSWSANSS VAGSTSSSLCEHWVSRLPGSKP ASVTSAASSRRTSLASLSESVE MTGERSEDDGGFSTRPFVRSVQ RQSLSSRSSVTSPLAVNENCMR PSWSLSAKLQMRSNSPSRFSGD SPIHSSASTLEKIG EAADDKVSISCFGSLRNLSSSY QEPSDSHSRREHKAVGRAPLAV MEGVFKDESDTRRLNSSVVDTQ SKHSAQGDRLPPLSGPFDNNNQ IAYVDQSDSVDSSPVKEVKAPS HPGSLAKKPESTTKRSPSSKGT SEPEKSLRKGRPALASQESSLS STSPSSPLPVKVSLKPSRSRSK ADSSSRGSGRHSSPAPAQPKKE SSPKSQDSVSSPSPQKQKSASA LTYTASSTSAKKASGPATRSPF PPGKSRTSDHSLSREGSRQSLG SDRASATSTSKPNSPRVSQARA GEGRGAGKHVRSSS MASLRSPSTSIKSGLKRDSKSE DKGLSFFKSALRQKETRRSTDL GKTALLSKKAGGSSVKSVCKNT GDDEAERGHQPPASQQPNANTT GKEQLVTKDPASAKHSLLSARK		TVVYQGKCSHCMRIGVAVPL SGTVARLREAVSMETKIPTD QIVLTEMYYDGFHRSFCDTD DLETVHESDCIFAFETPEIF RPEGILSQRGIHLNNNLNHL KFGLDYHRLSSPTQTAAKQG KMDSPTSRAGSDKIVLLVCN RACTGQQGKRFGLPFVLHLE KTIAWDLLQKEILEKMKYFL RPTVCIQVCPFSLRVVSVVG ITYLLPQEEQPLCHPIVE RALKSCGPGGTAHVKLVVEW DKETRDFLFVNTEDEYIPDA ESVRLQRERHHQPQTCTLSQ CFQLYTKEERLAPDDAWRCP HCKQLQQGSITLSLWTLPDV LIIHLKRFRQEGDRRMKLQN MVKFPLTGLDMTPHVVKRSQ SSWSLPSHWSPWRRPYGLGR DPEDYIYDLYAVCNHHGTMQ GGHYTAYCKNSVDGLWYCFD DSDVQQLSEDEVCTQTAYIL FYQRRT

		SKSSQLDSGVPSSPGGRQSAEK SSKKLSSSMQTSARPSQKPQ		
U17LJ_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 19	40	MEEDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KTLTLHTSAKVLILVLKRFSDV TGNKIAKNVQYPEC	152	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQTNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS EWERHSESVSRGREPRALGA EDTDRRATQGELKRDHPCLQ APEL
		LDMQPYMSQTNTGPLVYVLYAV LVHAGWSCHNGHYFSYVKAQEG QWYKMDDAEVTASSITSVLSQQ AYVLFYIQKSEWERHSESVSRG REPRALGAEDTDRRATQGELKR DHPCLQAPELDEHLVERATQES TLDHWKFLQEQNKTKPEFNVRK VEGTLPPDVLVIHQSKYKCGMK NHHPEQQSSLLKLSSTTPTHQE SMNTGTLASLRGRARRSKGKNK HSKRALLVCQ		
U17LF_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 15	41	MEDDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KTLTLHTSAKVLILVLKRFSDV TGNKIDKNVQYPEC	153	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKIDKNVQ YPECLDMKLYMSQTNSGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS
		LDMKLYMSQTNSGPLVYVLYAV LVHAGWSCHNGHYFSYVKAQEG QWYKMDDAEVTASSITSVLSQQ AYVLFYIQKSEWERHSESVSRG REPRALGAEDTDRRATQGELKR DHPCLQAPELDEHLVERATQES TLDHWKFLQEQNKTKPEFNVRK VEGTLPPDVLVIHQSKYKCGMK NHHPEQQSSLLNLSSTTPTHQE SMNTGTLASLRGRARRSKGKNK		

		HSKRALLVCQWSQWKYRPTRRG AHTHAHTQTHT		
UBP47_HUMAN Ubiquitin carboxyl-terminal hydrolase 47	42	MVPGEENQLVPKEDVFWRCRQN IFDEMKKKFLQIENAAEEPRVL CIIQDTTNSKTVNERITLNLPA STPVRKLFEDVANKVGYINGTF DLVWGNGINTADMAPLDHTSDK SLLDANFEPGKKNFLHLTDKDG EQPQILLEDSSAGEDSVHDRFI GPLPREGSGGSTSDYVSQSYSY SSILNKSETGYVGLVNQAMTCY LNSLLQTLFMTPEFRNALYKWE FEESEEDPVTSIPYQLQRLFVL LQTSKKRAIETTDVTRSFGWDS SEAWQQHDVQELCRVMFDALEQ KWKQTEQADLINEL YQGKLKDYVRCLECGYEGWRID TYLDIPLVIRPYGSSQAFASVE EALHAFIQPEILDGPNQYFCER CKKKCDARKGLRFLHFPYLLTL QLKRFDFDYTTMHRIKLNDRMT FPEELDMSTFIDVEDEKSPQTE SCTDSGAENEGSCHSDQMSNDF SNDDGVDEGICLETNSGTEKIS KSGLEKNSLIYELFSVMVHSGS AAGGHYYACIKSFSDEQWYSFN DQHVSRITQEDIKKTHGGSSGS RGYYSSAFASSTNAYMLIYRLK DPARNAKFLEVDEYPEHIKNLV QKERELEEQEKRQR EIERNTCKIKLFCLHPTKQVMM ENKLEVHKDKTLKEAVEMAYKM MDLEEVIPLDCCRLVKYDEFHD YLERSYEGEEDTPMGLLLGGVK STYMFDLLLETRKPDQVFQSYK PGEVMVKVHVVDLKAESVAAPI TVRAYLNQTVTEFKQLISKAIH LPAETMRIVLERCYNDLRLLSV SSKTLKAEGFFRSNKVFVESSE TLDYQMAFADSHLWKLLDRHAN TIRLFVLLPEQSPVSYSKRTAY QKAGGDSGNVDDDCERVKGPVG SLKSVEAILEESTEKLKSLSLQ QQQDGDNGDSSKST ETSDFENIESPLNERDSSASVD NRELEQHIQTSDPENFQSEERS DSDVNNDRSTSSVDSDILSSSH SSDTLCNADNAQIPLANGLDSH SITSSRRTKANEGKKETWDTAE EDSGTDSEYDESGKSRGEMQYM YFKAEPYAADEGSGEGHKWLMV	154	ETGYVGLVNQAMTCYLNSLL QTLFMTPEFRNALYKWEFEE SEEDPVTSIPYQLQRLFVLL QTSKKRAIETTDVTRSFGWD SSEAWQQHDVQELCRVMFDA LEQKWKQTEQADLINELYQG KLKDYVRCLECGYEGWRIDT YLDIPLVIRPYGSSQAFASV EEALHAFIQPEILDGPNQYF CERCKKKCDARKGLRFLHFP YLLTLQLKRFDFDYTTMHRI KLNDRMTFPEELDMSTFIDV EDEKSPQTESCTDSGAENEG SCHSDQMSNDFSNDDGVDEG ICLETNSGTEKISKSGLEKN SLIYELFSVMVHSGSAAGGH YYACIKSFSDEQWYSFNDQH VSRITQEDIKKTHGGSSGSR GYYSSAFASSTNAYMLIYRL KD

		HVDKRITLAAFKQHLEPFVGVL SSHFKVFRVYASNQEFESVRLN ETLSSFSDDNKITIRLGRALKK GEYRVKVYQLLVNEQEPCKFLL DAVFAKGMTVRQSKEELIPQLR EQCGLELSIDRFRLRKKTWKNP GTVFLDYHIYEEDI NISSNWEVFLEVLDGVEKMKSM SQLAVLSRRWKPSEMKLDPFQE VVLESSSVDELREKLSEISGIP LDDIEFAKGRGTFPCDISVLDI HQDLDWNPKVSTLNVWPLYICD DGAVIFYRDKTEELMELTDEQR NELMKKESSRLQKTGHRVTYSP RKEKALKIYLDGAPNKDLTQD		
UBP51_HUMAN Ubiquitin carboxyl-terminal hydrolase 51	43	MAQVRETSLPSGSGVRWISGGG GGASPEEAVEKAGKMEEAAAGA TKASSRREAEEMKLEPLQEREP APEENLTWSSSGGDEKVLPSIP LRCHSSSSPVCPRRKPRPRPQP RARSRSQPGLSAPPPPPARPPP PPPPPPPPAPRPRAWRGSRRRS RPGSRPQTRRSCSGDLDGSGDP GGLGDWLLEVEFGQGPTGCSHV ESFKVGKNWQKNLRLIYQRFVW SGTPETRKRKAKSCICHVCSTH MNRLHSCLSCVFFGCFTEKHIH KHAETKQHHLAVDLYHGVIYCF MCKDYVYDKDIEQI AKETKEKILRLLTSTSTDVSHQ QFMTSGFEDKQSTCETKEQEPK LVKPKKKRRKKSVYTVGLRGLI NLGNTCFMNCIVQALTHIPLLK DFFLSDKHKCIMTSPSLCLVCE MSSLFHAMYSGSRTPHIPYKLL HLIWIHAEHLAGYRQQDAHEFL IAILDVLHRHSKDDSGGQEANN PNCCNCIIDQIFTGGLQSDVTC QACHSVSTTIDPCWDISLDLPG SCATFDSQNPERADSTVSRDDH IPGIPSLTDCLQWFTRPEHLGS SAKIKCNSCQSYQESTKQLTMK KLPIVACFHLKRFE HVGKQRRKINTFISFPLELDMT PFLASTKESRMKEGQPPTDCVP NENKYSLFAVINHHGTLESGHY TSFIRQQKDQWFSCDDAIITKA TIEDLLYSEGYLLFYHKQGLEK D	155	YTVGLRGLINLGNTCFMNCI VQALTHIPLLKDFFLSDKHK CIMTSPSLCLVCEMSSLFHA MYSGSRTPHIPYKLLHLIWI HAEHLAGYRQQDAHEFLIAI LDVLHRHSKDDSGGQEANNP NCCNCIIDQIFTGGLQSDVT CQACHSVSTTIDPCWDISLD LPGSCATFDSQNPERADSTV SRDDHIPGIPSLTDCLQWFT RPEHLGSSAKIKCNSCQSYQ ESTKQLTMKKLPIVACFHLK RFEHVGKQRRKINTFISFPL ELDMTPFLASTKESRMKEGQ PPTDCVPNENKYSLFAVINH HGTLESGHYTSFIRQQKDQW FSCDDAIITKATIEDLLYSE GYLLFYHKQG
UBP36_HUMAN Ubiquitin	44	MPIVDKLKEALKPGRKDSADDG ELGKLLASSAKKVLLQKIEFEP	156	RVGAGLHNLGNTCFLNATIQ CLTYTPPLANYLLSKEHARS

carboxyl-terminal hydrolase 36		ASKSFSYQLEALKSKYVLLNPK TEGASRHKSGDDPPARRQGSEH TYESCGDGVPAPQKVLFPTERL SLRWERVFRVGAGLHNLGNTCF LNATIQCLTYTPPLANYLLSKE HARSCHQGSFCMLCVMQNHIVQ AFANSGNAIKPVSFIRDLKKIA RHFRFGNQEDAHEFLRYTIDAM QKACLNGCAKLDRQTQATTLVH QIFGGYLRSRVKCSVCKSVSDT YDPYLDVALEIRQAANIVRALE LFVKADVLSGENAY MCAKCKKKVPASKRFTIHRTSN VLTLSLKRFANFSGGKITKDVG YPEFLNIRPYMSQNNGDPVMYG LYAVLVHSGYSCHAGHYYCYVK ASNGQWYQMNDSLVHSSNVKVV LNQQAYVLFYLRIPGSKKSPEG LISRTGSSSLPGRPSVIPDHSK KNIGNGIISSPLTGKRQDSGTM KKPHTTEEIGVPISRNGSTLGL KSQNGCIPPKLPSGSPSPKLSQ TPTHMPTILDDPGKKVKKPAPP QHFSPRTAQGLPGTSNSNSSRS GSQRQGSWDSRDVVLSTSPKLL ATATANGHGLKGND ESAGLDRRGSSSSSPEHSASSD STKAPQTPRSGAAHLCDSQETN CSTAGHSKTPPSGADSKTVKLK SPVLSNTTTEPASTMSPPPAKK LALSAKKASTLWRATGNDLRPP PPSPSSDLTHPMKTSHPVVAST WPVHRARAVSPAPQSSSRLQPP FSPHPTLLSSTPKPPGTSEPRS CSSISTALPQVNEDLVSLPHQL PEASEPPQSPSEKRKKTFVGEP QRLGSETRLPQHIREATAAPHG KRKRKKKKRPEDTAASALQEGQ TQRQPGSPMYRREGQAQLPAVR RQEDGTQPQVNGQQ VGCVTDGHHASSRKRRRKGAEG LGEEGGLHQDPLRHSCSPMGDG DPEAMEESPRKKKKKKRKQETQ RAVEEDGHLKCPRSAKPQDAVV PESSSCAPSANGWCPGDRMGLS QAPPVSWNGERESDVVQELLKY SSDKAYGRKVLTWDGKMSAVSQ DAIEDSRQARTETVVDDWDEEF DRGKEKKIKKFKREKRRNFNAF QKLQTRRNFWSVTHPAKAASLS YRR		CHQGSFCMLCVMQNHIVQAF ANSGNAIKPVSFIRDLKKIA RHFRFGNQEDAHEFLRYTID AMQKACLNGCAKLDRQTQAT TLVHQIFGGYLRSRVKCSVC KSVSDTYDPYLDVALEIRQA ANIVRALELFVKADVLSGEN AYMCAKCKKKVPASKRFTIH RTSNVLTLSLKRFANFSGGK ITKDVGYPEFLNIRPYMSQN NG DPVMYGLYAVLVHSGYSCHA GHYYCYVKASNGQWYQMNDS LVHSSNVKVVLNQQAYVLFY LRIP

UBP44_HUMAN Ubiquitin carboxyl-terminal hydrolase 44	45	MLAMDTCKHVGQLQLAQDHSSL NPQKWHCVDCNTTESIWACLSC SHVACGRYIEEHALKHFQESSH PVALEVNEMYVFCYLCDDYVLN DNTTGDLKLLRRTLSAIKSQNY HCTTRSGRFLRSMGTGDDSYFL HDGAQSLLQSEDQLYTALWHRR RILMGKIFRTWFEQSPIGRKKQ EEPFQEKIVVKREVKKRRQELE YQVKAELESMPPRKSLRLQGLA QSTIIEIVSVQVPAQTPASPAK DKVLSTSENEISQKVSDSSVKR RPIVTPGVTGLRNLGNTCYMNS VLQVLSHLLIFRQC FLKLDLNQWLAMTASEKTRSCK HPPVTDTVVYQMNECQEKDTGF VCSRQSSLSSGLSGGASKGRKM ELIQPKEPTSQYISLCHELHTL FQVMWSGKWALVSPFAMLHSVW RLIPAFRGYAQQDAQEFLCELL DKIQRELETTGTSLPALIPTSQ RKLIKQVLNVVNNIFHGQLLSQ VTCLACDNKSNTIEPFWDLSLE FPERYQCSGKDIASQPCLVTEM LAKFTETEALEGKIYVCDQCNS KRRRFSSKPVVLTEAQKQLMIC HLPQVLRLHLKRFRWSGRNNRE KIGVHVGFEEILNM EPYCCRETLKSLRPECFIYDLS AVVMHHGKGFGSGHYTAYCYNS EGGFWVHCNDSKLSMCTMDEVC KAQAYILFYTQRVTENGHSKLL PPELLLGSQHPNEDADTSSNEI LS	157	TPGVTGLRNLGNTCYMNSVL QVLSHLLIFRQCFLKLDLNQ WLAMTASEKTRSCKHPPVTD TVVYQMNECQEKDTGFVCSR QSSLSSGLSGGASKGRKMEL IQPKEPTSQYISLCHELHTL FQVMWSGKWALVSPFAMLHS VWRLIPAFRGYAQQDAQEFL CELLDKIQRELETTGTSLPA LIPTSQRKLIKQVLNVVNNI FHGQLLSQVTCLACDNKSNT IEPFWDLSLEFPERYQCSGK DIASQPCLVTEMLAKFTETE ALEGKIYVCDQCNSKRRRFS SKPVVLTEAQKQLMICHLPQ VLRLHLKRFRWSGRNNREKI GVHVGFEEILNMEPYCCRET LKSLRPECFIYDLSAVVMHH GKGFGSGHYTAYCYNSEGGF WVHCNDSKLSMCTMDEVCKA QAYILFYTQRV
UBP8_HUMAN Ubiquitin carboxyl-terminal hydrolase 8	46	MPAVASVPKELYLSSSLKDLNK KTEVKPEKISTKSYVHSALKIF KTAEECRLDRDEERAYVLYMKY VTVYNLIKKRPDFKQQQDYFHS ILGPGNIKKAVEEAERLSESLK LRYEEAEVRKKLEEKDRQEEAQ RLQQKRQETGREDGGTLAKGSL ENVLDSKDKTQKSNGEKNEKCE TKEKGAITAKELYTMMTDKNIS LIIMDARRMQDYQDSCILHSLS VPEEAISPGVTASWIEAHLPDD SKDTWKKRGNVEYVVLLDWFSS AKDLQIGTTLRSLKDALFKWES KTVLRNEPLVLEGG YENWLLCYPQYTTNAKVTPPPR RQNEEVSISLDFTYPSLEESIP SKPAAQTPPASIEVDENIELIS	158	PALTGLRNLGNTCYMNSILQ CLCNAPHLADYFNRNCYQDD INRSNLLGHKGEVAEEFGII MKALWTGQYRYISPKDFKIT IGKINDQFAGYSQQDSQELL LFLMDGLHEDLNKADNRKRY KEENNDHLDDFKAAEHAWQK HKQLNESIIVALFQGQFKST VQCLTCHKKSRTFEAFMYLS LPLASTSKCTLQDCLRLFSK EEKLTDNNRFYCSHCRARRD SLKKIEIWKLPPVLLVHLKR FSYDGRWKQKLQTSVDFPLE NLDLSQYVIGPKNNLKKYNL FSVSNHYGGLDGGHYTAYCK NAARQRWFKFDDHEVSDISV SSVKSSAAYILFYTSLG

		GQNERMGPLNISTPVEPVAASK SDVSPIIQPVPSIKNVPQIDRT KKPAVKLPEEHRIKSESTNHEQ QSPQSGKVIPDRSTKPVVFSPT LMLTDEEKARIHAETALLMEKN KQEKELRERQQEEQKEKLRKEE QEQKAKKKQEAEENEITEKQQK AKEEMEKKESEQAKKEDKETSA KRGKEITGVKRQSKSEHETSDA KKSVEDRGKRCPTPEIQKKSTG DVPHTSVTGDSGSG KPFKIKGQPESGILRTGTFRED TDDTERNKAQREPLTRARSEEM GRIVPGLPSGWAKFLDPITGTF RYYHSPTNTVHMYPPEMAPSSA PPSTPPTHKAKPQIPAERDREP SKLKRSYSSPDITQAIQEEEKR KPTVTPTVNRENKPTCYPKAEI SRLSASQIRNLNPVFGGSGPAL TGLRNLGNTCYMNSILQCLCNA PHLADYFNRNCYQDDINRSNLL GHKGEVAEEFGIIMKALWTGQY RYISPKDFKITIGKINDQFAGY SQQDSQELLLFLMDGLHEDLNK ADNRKRYKEENNDH LDDFKAAEHAWQKHKQLNESII VALFQGQFKSTVQCLTCHKKSR TFEAFMYLSLPLASTSKCTLQD CLRLFSKEEKLTDNNRFYCSHC RARRDSLKKIEIWKLPPVLLVH LKRFSYDGRWKQKLQTSVDFPL ENLDLSQYVIGPKNNLKKYNLF SVSNHYGGLDGGHYTAYCKNAA RQRWFKFDDHEVSDISVSSVKS SAAYILFYTSLGPRVTDVAT		
UBP37_HUMAN Ubiquitin carboxyl-terminal hydrolase 37	47	MSPLKIHGPIRIRSMQTGITKW KEGSFEIVEKENKVSLVVHYNT GGIPRIFQLSHNIKNVVLRPSG AKQSRLMLTLQDNSFLSIDKVP SKDAEEMRLFLDAVHQNRLPAA MKPSQGSGSFGAILGSRTSQKE TSRQLSYSDNQASAKRGSLETK DDIPFRKVLGNPGRGSIKTVAG SGIARTIPSLTSTSTPLRSGLL ENRTEKRKRMISTGSELNEDYP KENDSSSNNKAMTDPSRKYLTS SREKQLSLKQSEENRTSGLLPL QSSSFYGSRAGSKEHSSGGTNL DRTNVSSQTPSAKR SLGFLPQPVPLSVKKLRCNQDY TGWNKPRVPLSSHQQQQLQGFS	159	QQLQGFSNLGNTCYMNAILQ SLFSLQSFANDLLKQGIPWK KIPLNALIRRFAHLLVKKDI CNSETKKDLLKKVKNAISAT AERFSGYMQNDAHEFLSQCL DQLKEDMEKLNKTWKTEPVS GEENSPDISATRAYTCPVIT NLEFEVQHSIICKACGEIIP KREQFNDLSIDLPRRKKPLP PRSIQDSLDLFFRAEELEYS CEKCGGKCALVRHKFNRLPR VLILHLKRYSFNVALSLNNK IGQQVIIPRYLTLSSHCTEN TKP PFTLGWSAHMAISRPLKASQ MVNSCITSPSTPSKKFTFKS

		NLGNTCYMNAILQSLFSLQSFA NDLLKQGIPWKKIPLNALIRRF AHLLVKKDICNSETKKDLLKKV KNAISATAERFSGYMQNDAHEF LSQCLDQLKEDMEKLNKTWKTE PVSGEENSPDISATRAYTCPVI TNLEFEVQHSIICKACGEIIPK REQFNDLSIDLPRRKKPLPPRS IQDSLDLFFRAEELEYSCEKCG GKCALVRHKFNRLPRVLILHLK RYSFNVALSLNNKIGQQVIIPR YLTLSSHCTENTKP PFTLGWSAHMAISRPLKASQMV NSCITSPSTPSKKFTFKSKSSL ALCLDSDSEDELKRSVALSQRL CEMLGNEQQQEDLEKDSKLCPI EPDKSELENSGFDRMSEEELLA AVLEISKRDASPSLSHEDDDKP TSSPDTGFAEDDIQEMPENPDT METEKPKTITELDPASFTEITK DCDENKENKTPEGSQGEVDWLQ QYDMERE REEQELQQALAQSLQ EQEAWEQKEDDDLKRATELSLQ EFNNSFVDALGSDEDSGNEDVF DMEYTEAEAEELKRNAETGNLP HSYRLISVVSHIGS TSSSGHYISDVYDIKKQAWFTY NDLEVSKIQEAAVQSDRDRSGY IFFYMHKEIFDELLETEKNSQS LSTEVGKTTRQAL		KSSLALCLDSDSEDELKRSV ALSQRLCEMLGNEQQQEDLE KDSKLCPIEPDKSELENSGF DRMSEEELLAAVLEISKRDA SPSLSHEDDDKPTSSPDTGF AEDDIQEMPENPDTMETEKP KTITELDPASFTEITKDCDE NKENKTPEGSQGEVDWLQQY DMERE REEQELQQALAQSLQ EQEAWEQKEDDDLKRATELS LQEFNNSFVDALGSDEDSGN EDVFDMEYTEAEAEELKRNA ETGNLPHSYRLISVVSHIGS TSSSGHYISDVYDIKKQAWF TYNDLEVSKIQEAAVQSDRD RSGYIFFYMHK
U17LD_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 13	48	MEEDSLYLGGEWQFNHFSKLTS SRLDAAFAEIQRTSLPEKSPLS CETRVDLCDDLVPEARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHPSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KTLTLHTSAKVLILVLKRFSDV TGNKIAKNVQYPEC LDMQPYMSQQNTGPLVYVLYAV LVHAGWSCHNGHYFSYVKAQEG QWYKMDDAEVTAASITSVLSQQ AYVLFYIQKSEWERHSESVSRG REPRALGAEDTDRRATQGELKR DHPCLQAPELDEHLVERATQES TLDRWKFLQEQNKTKPEFNVRK	160	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHPSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQQNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA ASITSVLSQQAYVLFYIQKS

		VEGTLPPDVLVIHQSKYKCGMK NHHPEQQSSLLNLSSSTPTHQE SMNTGTLASLRGRARRSKGKNK HSKRALLVCQ		
U17L3_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 3	49	MGDDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS SETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYENASLQCLTYTLPLANYMLS REHSQTCQRPKCCMLCTMQAHI TWALHSPGHVIQPSQALASGFH RGKQEDVHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GCWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVKQALEQLVK PEELNGENAYHCGLCLQRAPAS NTLTLHTSAKVLILVLKRFSDV AGNKLAKNVQYPEC LDMQPYMSQQNTGPLVYVLYAV LVHAGWSCHDGHYFSYVKAQEG QWYKMDDAEVTVCSITSVLSQQ AYVLFYIQKSEWERHSESVSRG REPRALGAEDTDRRAKQGELKR DHPCLQAPELDEHLVERATQES TLDHWKFLQEQNKTKPEFNVGK VEGTLPPNALVIHQSKYKCGMK NHHPEQQSSLLNLSSTTRTDQE SMNTGTLASLQGRTRRAKGKNK HSKRALLVCQ	161	AVGAGLQNMGNTCYENASLQ CLTYTLPLANYMLSREHSQT CQRPKCCMLCTMQAHITWAL HSPGHVIQPSQALASGFHRG KQEDVHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGCWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVKQA LEQLVKPEELNGENAYHCGL CLQRAPASNTLTLHTSAKVL ILVLKRFSDVAGNKLAKNVQ YPECLDMQPYMSQQNTGPLV YVLYAVLVHAGWSCHDGHYF SYVKAQEGQWYKMDDAEVTV CSITSVLSQQAYVLFYIQKS
UBP54_HUMAN Inactive ubiquitin carboxyl-terminal hydrolase 54	50	MSWKRNYFSGGRGSVQGMFAPR SSTSIAPSKGLSNEPGQNSCFL NSALQVLWHLDIFRRSFRQLTT HKCMGDSCIFCALKGIFNQFQC SSEKVLPSDTLRSALAKTFQDE QRFQLGIMDDAAECFENLLMRI HFHIADETKEDICTAQHCISHQ KFAMTLFEQCVCTSCGATSDPL PFIQMVHYISTTSLCNQAICML ERREKPSPSMFGELLQNASTMG DLRNCPSNCGERIRIRRVLMNA PQIITIGLVWDSDHSDLAEDVI HSLGTCLKLGDLFFRVTDDRAK QSELYLVGMICYYG KHYSTFFFQTKIRKWMYFDDAH VKEIGPKWKDVVTKCIKGHYQP LLLLYADPQGTPVSTQDLPPQA EFQSYSRTCYDSEDSGREPSIS SDTRTDSSTESYPYKHSHHESV VSHFSSDSQGTVIYNVENDSMS QSSRDTGHLTDSECNQKHTSKK GSLIERKRSSGRVRRKGDEPQA	162	APSKGLSNEPGQNSCFLNSA LQVLWHLDIFRRSFRQLTTH KCMGDSCIFCALKGIFNQFQ CSSEKVLPSDTLRSALAKTF QDEQRFQLGIMDDAAECFEN LLMRIHFHIADETKEDICTA QHCISHQKFAMTLFEQCVCT SCGATSDPLPFIQ MVHYISTTSLCNQAICMLER REKPSPSMFGELLQNASTMG DLRNCPSNCGERIRIRRVLM NAPQIITIGLVWDSDHSDLA EDVIHSLGTCLKLGDLFFRV TDDRAKQSELYLVGMICYYG KHYSTFFFQTKIRKWMYFDD AHVKEIGPKWKDVVTKCIKG HYQPLLLLYADPQGTPVSTQ DLPPQAEFQSYSRTCYDSED SGREPSISSDTRTDSSTESY PYKHSHHESVVSHFSSDSQG TVIYNVEND

		SGYHSEGETLKEKQAPRNASKP SSSTNRLRDFKETVSNMIHNRP SLASQTNVGSHCRGRGGDQPDK KPPRTLPLHSRDWEIESTSSES KSSSSSKYRPTWRPKRESLNID SIFSKDKRKHCGYT QLSPFSEDSAKEFIPDEPSKPP SYDIKFGGPSPQYKRWGPARPG SHLLEQHPRLIQRMESGYESSE RNSSSPVSLDAALPESSNVYRD PSAKRSAGLVPSWRHIPKSHSS SILEVDSTASMGGWTKSQPFSG EEISSKSELDELQEEVARRAQE QELRRKREKELEAAKGFNPHPS RFMDLDELQNQGRSDGFERSLQ EAESVFEESLHLEQKGDCAAAL ALCNEAISKLRLALHGASCSTH SRALVDKKLQISIRKARSLQDR MQQQQSPQQPSQPSACLPTQAG TLSQPTSEQPIPLQ VLLSQEAQLESGMDTEFGASSF FHSPASCHESHSSLSPESSAPQ HSSPSRSALKLLTSVEVDNIEP SAFHRQGLPKAPGWTEKNSHHS WEPLDAPEGKLQGSRCDNSSCS KLPPQEGRGIAQEQLFQEKKDP ANPSPVMPGIATSERGDEHSLG CSPSNSSAQPSLPLYRTCHPIM PVASSFVLHCPDPVQKTNQCLQ GQSLKTSLTLKVDRGSEETYRP EFPSTKGLVRSLAEQFQRMQGV SMRDSTGFKDRSLSGSLRKNSS PSDSKPPFSQGQEKGHWPWAKQ QSSLEGGDRPLSWE ESTEHSSLALNSGLPNGETSSG GQPRLAEPDIYQEKLSQVRDVR SKDLGSSTDLGTSLPLDSWVNI TRFCDSQLKHGAPRPGMKSSPH DSHTCVTYPERNHILLHPHWNQ DTEQETSELESLYQASLQASQA GCSGWGQQDTAWHPLSQTGSAD GMGRRLHSAHDPGLSKTSTAEM EHGLHEARTVRTSQATPCRGLS RECGEDEQYSAENLRRISRSLS GTVVSEREEAPVSSHSFDSSNV RKPLETGHRCSSSSSLPVIHDP SVFLLGPQLYLPQPQFLSPDVL MPTMAGEPNRLPGT SRSVQQFLAMCDRGETSQGAKY TGRTLNYQSLPHRSRTDNSWAP WSETNQHIGTRFLTTPGCNPQL		

		TYTATLPERSKGLQVPHTQSWS DLFHSPSHPPIVHPVYPPSSSL HVPLRSAWNSDPVPGSRTPGPR RVDMPPDDDWRQSSYASHSGHR RTVGEGFLFVLSDAPRREQIRA RVLQHSQW		
SNUT2_HUMAN U4/U6.U5 tri-snRNP-associated protein 2	51	MSGRSKRESRGSTRGKRESESR GSSGRVKRERDREREPEAASSR GSPVRVKREFEPASAREAPASV VPFVRVKREREVDEDSEPEREV RAKNGRVDSEDRRSRHCPYLDT INRSVLDFDFEKLCSISLSHIN AYACLVCGKYFQGRGLKSHAYI HSVQFSHHVFLNLHTLKFYCLP DNYEIIDSSLEDITYVLKPTFT KQQIANLDKQAKLSRAYDGTTY LPGIVGLNNIKANDYANAVLQA LSNVPPLRNYFLEEDNYKNIKR PPGDIMFLLVQRFGELMRKLWN PRNFKAHVSPHEML QAVVLCSKKTFQITKQGDGVDF LSWFLNALHSALGGTKKKKKTI VTDVFQGSMRIFTKKLPHPDLP AEEKEQLLHNDEYQETMVESTF MYLTLDLPTAPLYKDEKEQLII PQVPLFNILAKFNGITEKEYKT YKENFLKRFQLTKLPPYLIFCI KRFTKNNFFVEKNPTIVNFPIT NVDLREYLSEEVQAVHKNTTYD LIANIVHDGKPSEGSYRIHVLH HGTGKWYELQDLQVTDILPQMI TLSEAYIQIWKRRDNDETNQQG A	163	LPGIVGLNNIKANDYANAVL QALSNVPPLRNYFLEEDNYK NIKRPPGDIMFLLVQRFGEL MRKLWNPRNFKAHVSPHEML QAVVLCSKKTFQITKQGDGV DFLSWFLNALHSALGGTKKK KKTIVTDVFQGSMRIFTKKL PHPDLPAEEKEQLLHNDEYQ ETMVESTFMYLTLDLPTAPL YKDEKEQLIIPQVPLFNILA KFNGITEKEYKTYKENFLKR FQLTKLPPYLIFCIKRFTKN NFFVEKNPTIVNFPITNVDL REYLSEEVQAVHKNTTYDLI ANIVHDGKPSEGSYRIHVLH HGTGKWYELQDLQVTDILPQ MITLSEAYIQIWKRRD
UBP35_HUMAN Ubiquitin carboxyl-terminal hydrolase 35	52	MDKILEAVVTSSYPVSVKQGLV RRVLEAARQPLEREQCLALLAL GARLYVGGAEELPRRVGCQLLH VAGRHHPDVFAEFFSARRVLRL LQGGAGPPGPRALACVQLGLQL LPEGPAADEVFALLRREVLRTV CERPGPAACAQVARLLARHPRC VPDGPHRLLFCQQLVRCLGRFR CPAEGEEGAVEFLEQAQQVSGL LAQLWRAQPAAILPCLKELFAV ISCAEEEPPSSALASVVQHLPL ELMDGVVRNLSNDDSVTDSQML TAISRMIDWVSWPLGKNIDKWI IALLKGLAAVKKFS ILIEVSLTKIEKVFSKLLYPIV RGAALSVLKYMLLTFQHSHEAF HLLLPHIPPMVASLVKEDSNSG TSCLEQLAELVHCMVFRFPGFP	164	SDTGKIGLINLGNTCYVNSI LQALFMASDFRHCVLRLTEN NSQPLMTKLQWLFGFLEHSQ RPAISPENFLSASWTPWFSP GTQQDCSEYLKYLLDRLHEE EKTGTRICQKLKQSSSPSPP EEPPAPSSTSVEKMFGGKIV TRICCLCCLNVSSREEAFTD LSLAFPPPERCRRRRLGSVM RPTEDITARELPPPTSAQGP GRVGPRRQRKHCITEDTPPT SLYIEGLDSKEAGGQSSQEE RIEREEEGKEERTEKEEVGE EEESTRGEGEREKEEEVEEE EEKVE KETEKEAEQEKEEDSLGAGT HPDAAIPSGERTCGSEGSRS VLDLVNYFLSPEKLTAENRY

		DLYEPVMEAIKDLHVPNEDRIK QLLGQDAWTSQKSELAGFYPRL MAKSDTGKIGLINLGNTCYVNS ILQALFMASDFRHCVLRLTENN SQPLMTKLQWLFGFLEHSQRPA ISPENFLSASWTPWFSPGTQQD CSEYLKYLLDRLHEEEKTGTRI CQKLKQSSSPSPPEEPPAPSST SVEKMFGGKIVTRICCLCCLNV SSREEAFTDLSLAF PPPERCRRRRLGSVMRPTEDIT ARELPPPTSAQGPGRVGPRRQR KHCITEDTPPTSLYIEGLDSKE AGGQSSQEERIEREEEGKEERT EKEEVGEEEESTRGEGEREKEE EVEEEEEKVEKETEKEAEQEKE EDSLGAGTHPDAAIPSGERTCG SEGSRSVLDLVNYFLSPEKLTA ENRYYCESCASLQDAEKVVELS QGPCYLILTLLRFSFDLRTMRR RKILDDVSIPLLLRLPLAGGRG QAYDLCSVVVHSGVSSESGHYY CYAREGAARPAASLGTADRPEP ENQWYLFNDTRVSF SSFESVSNVTSFFPKDTAYVLF YRQRPREGPEAELGSSRVRTEP TLHKDLMEAISKDNILYLQEQE KEARSRAAYISALPTSPHWGRG FDEDKDEDEGSPGGCNPAGGNG GDFHRLVF		YCESCASLQDAEKVVELSQG PCYLILTLLRFSFDLRTMRR RKILDDVSIPLLLRLPLAGG RGQAYDLCSVVVHSGVSSES GHYYCYAREGAARPAASLGT ADRPEPENQWYLFNDTRVSF SSFESVSNVTSFFPKDTAYV LFYRQRP
UBP15_HUMAN Ubiquitin carboxyl-terminal hydrolase 15	53	MAEGGAADLDTQRSDIATLLKT SLRKGDTWYLVDSRWFKQWKKY VGFDSWDKYQMGDQNVYPGPID NSGLLKDGDAQSLKEHLIDELD YILLPTEGWNKLVSWYTLMEGQ EPIARKVVEQGMFVKHCKVEVY LTELKLCENGNMNNVVTRRFSK ADTIDTIEKEIRKIFSIPDEKE TRLWNKYMSNTFEPLNKPDSTI QDAGLYQGQVLVIEQKNEDGTW PRGPSTPKSPGASNFSTLPKIS PSSLSNNYNNMNNRNVKNSNYC LPSYTAYKNYDYSEPGRNNEQP GLCGLSNLGNTCFM NSAIQCLSNTPPLTEYFLNDKY QEELNFDNPLGMRGEIAKSYAE LIKQMWSGKFSYVTPRAFKTQV GRFAPQFSGYQQQDCQELLAFL LDGLHEDLNRIRKKPYIQLKDA DGRPDKVVAEEAWENHLKRNDS IIVDIFHGLFKSTLVCPECAKI	165	EQPGLCGLSNLGNTCFMNSA IQCLSNTPPLTEYFLNDKYQ EELNFDNPLGMRGEIAKSYA ELIKQMWSGKFSYVTPRAFK TQVGRFAPQFSGYQQQDCQE LLAFLLDGLHEDLNRIRKKP YIQLKDADGRPDKVVAEEAW ENHLKRNDSIIVDIFHGLFK STLVCPECAKISVTFDPFCY LTLPLPMKKERTLEVYLVRM DPLTKPMQYKVVVPKIGNIL DLCTALSALSGIPADKMIVT DIYNHRFHRIFAMDENLSSI MERDDIYVFEININRTEDTE HVIIPVCLREKFRHSSYTHH TGSSLFGQPFLMAVPRNNTE DKLYNLLLLRMCRYVKISTE TEETEGSLHCCKDQNINGNG PNGIHEEGSPSEMETDEPDD ESSQDQELPSENENSQSEDS VGGDNDSENGLCTEDTCKGQ

		SVTFDPFCYLTLPLPMKKERTL EVYLVRMDPLTKPMQYKVVVPK IGNILDLCTALSALSGIPADKM IVTDIYNHRFHRIFAMDENLSS IMERDDIYVFEININRTEDTEH VIIPVCLREKFRHSSYTHHTGS SLFGQPFLMAVPRN NTEDKLYNLLLLRMCRYVKIST ETEETEGSLHCCKDQNINGNGP NGIHEEGSPSEMETDEPDDESS QDQELPSENENSQSEDSVGGDN DSENGLCTEDTCKGQLTGHKKR LFTFQFNNLGNTDINYIKDDTR HIRFDDRQLRLDERSFLALDWD PDLKKRYFDENAAEDFEKHESV EYKPPKKPFVKLKDCIELFTTK EKLGAEDPWYCPNCKEHQQATK KLDLWSLPPVLVVHLKRFSYSR YMRDKLDTLVDFPINDLDMSEF LINPNAGPCRYNLIAVSNHYGG MGGGHYTAFAKNKD DGKWYYFDDSSVSTASEDQIVS KAAYVLFYQRQDTFSGTGFFPL DRETKGASAATGIPLESDEDSN DNDNDIENENCMHTN		LTGHKKRLFTFQFNNLGNTD INYIKDDTRHIRFDDRQLRL DERSFLALDWDPDLKKRYFD ENAAEDFEKHESVEYKPPKK PFVKLKDCIELFTTKEKLGA EDPWYCPNCKEHQQATKKLD LWSLPPVLVVHLKRFSYSRY MRDKLDTLVDFPINDLDMSE FLINPNAGPCRYNLIAVSNH YGGMGGGHYTAFAKNKDDGK WYYFDDSSVSTASEDQIVSK AAYVLFYQRQD
UBP29_HUMAN Ubiquitin carboxyl-terminal hydrolase 29	54	MISLKVCGFIQIWSQKTGMTKL KEALIETVQRQKEIKLVVTFKS GKFIRIFQLSNNIRSVVLRHCK KRQSHLRLTLKNNVFLFIDKLS YRDAKQLNMFLDIIHQNKSQQP MKSDDDWSVFESRNMLKEIDKT SFYSICNKPSYQKMPLFMSKSP THVKKGILENQGGKGQNTLSSD VQTNEDILKEDNPVPNKKYKTD SLKYIQSNRKNPSSLEDLEKDR DLKLGPSFNTNCNGNPNLDETV LATQTLNAKNGLTSPLEPEHSQ GDPRCNKAQVPLDSHSQQLQQG FPNLGNTCYMNAVL QSLFAIPSFADDLLTQGVPWEY IPFEALIMTLTQLLALKDFCST KIKRELLGNVKKVISAVAEIFS GNMQNDAHEFLGQCLDQLKEDM EKLNATLNTGKECGDENSSPQM HVGSAATKVFVCPVVANFEFEL QLSLICKACGHAVLKVEPNNYL SINLHQETKPLPLSIQNSLDLF FKEEELEYNCQMCKQKSCVARH TFSRLSRVLIIHLKRYSFNNAW LLVKNNEQVYIPKSLSLSSYCN ESTKPPLPLSSSAPVGKCEVLE	166	QLQQGFPNLGNTCYMNAVLQ SLFAIPSFADDLLTQGVPWE YIPFEALIMTLTQLLALKDF CSTKIKRELLGNVKKVISAV AEIFSGNMQNDAHEFLGQCL DQLKEDMEKLNATLNTGKEC GDENSSPQMHVGSAATKVFV CPVVANFEFELQLSLICKAC GHAVLKVEPNNYLSINLHQE TKPLPLSIQNSLDLFFKEEE LEYNCQMCKQKSCVARHTFS RLSRVLIIHLKRYSFNNAWL LVKNNEQVYIPKSLSLSSYC NESTKPPLPLSSSAPVGKCE VLEVSQEMISEINSPLTPSM KLTSESSDSLVLPVEPDKNA DLQRFQRDCGDASQEQHQRD LENGSALESELVHFRDRAIG EKELPVADSLMDQGDISLPV MYEDGGKLISSPDTRLVEVH LQEVPQHPELQKYEKTNTFV EFNFDSVTESTNGFYDCKEN RIPEGSQGMAEQLQQCIEES IIDEFLQQAPPPGVRKLDAQ EHTEETLNQSTELRLQKADL NHLGALGSDNPGNKNILDAE

		VSQEMISEINSPLTPSMKLTSE SSDSLVLPVEPDKN ADLQRFQRDCGDASQEQHQRDL ENGSALESELVHFRDRAIGEKE LPVADSLMDQGDISLPVMYEDG GKLISSPDTRLVEVHLQEVPQH PELQKYEKTNTFVEFNFDSVTE STNGFYDCKENRIPEGSQGMAE QLQQCIEESIIDEFLQQAPPPG VRKLDAQEHTEETLNQSTELRL QKADLNHLGALGSDNPGNKNIL DAENTRGEAKELTRNVKMGDPL QAYRLISVVSHIGSSPNSGHYI SDVYDFQKQAWFTYNDLCVSEI SETKMQEARLHSGYIFFYMHNG IFEELLRKAENSRLPSTQAGVI PQGEYEGDSLYRPA		NTRGEAKELTRNVKMGDPLQ AYRLISVVSHIGSSPNSGHY ISDVYDFQKQAWFTYNDLCV SEISETKMQEARLHSGYIFF YMHN
UBP6_HUMAN Ubiquitin carboxyl-terminal hydrolase 6	55	MDMVENADSLQAQERKDILMKY DKGHRAGLPEDKGPEPVGINSS IDRFGILHETELPPVTAREAKK IRREMTRTSKWMEMLGEWETYK HSSKLIDRVYKGIPMNIRGPVW SVLLNIQEIKLKNPGRYQIMKE RGKRSSEHIHHIDLDVRTTLRN HVFFRDRYGAKQRELFYILLAY SEYNPEVGYCRDLSHITALFLL YLPEEDAFWALVQLLASERHSL PGFHSPNGGTVQGLQDQQEHVV PKSQPKTMWHQDKEGLCGQCAS LGCLLRNLIDGISLGLTLRLWD VYLVEGEQVLMPIT SIALKVQQKRLMKTSRCGLWAR LRNQFFDTWAMNDDTVLKHLRA STKKLTRKQGDLPPPAKREQGS LAPRPVPASRGGKTLCKGYRQA PPGPPAQFQRPICSASPPWASR FSTPCPGGAVREDTYPVGTQGV PSLALAQGGPQGSWRFLEWKSM PRLPTDLDIGGPWFPHYDFEWS CWVRAISQEDQLATCWQAEHCG EVHNKDMSWPEEMSFTANSSKI DRQKVPTEKGATGLSNLGNTCF MNSSIQCVSNTQPLTQYFISGR HLYELNRTNPIGMKGHMAKCYG DLVQELWSGTQKSV APLKLRRTIAKYAPKFDGFQQQ DSQELLAFLLDGLHEDLNRVHE KPYVELKDSDGRPDWEVAAEAW DNHLRRNRSIIVDLFHGQLRSQ VKCKTCGHISVRFDPFNFLSLP LPMDSYMDLEITVIKLDGTTPV	167	KGATGLSNLGNTCFMNSSIQ CVSNTQPLTQYFISGRHLYE LNRTNPIGMKGHMAKCYGDL VQELWSGTQKSVAPLKLRRT IAKYAPKFDGFQQQDSQELL AFLLDGLHEDLNRVHEKPYV ELKDSDGRPDWE VAAEAWDNHLRRNRSIIVDL FHGQLRSQVKCKTCGHISVR FDPNFLSLPLPMDSYMDLEI TVIKLDGTTPVRYGLRLNMD EKYTGLKKQLRDLCGLNSEQ ILLAEVHDSNIKNFPQDNQK VQLSVSGFLCAFEIPVPSSP ISASSPTQIDFSSSPSTNGM FTLTTNGDLPKPIFIPNGMP NTVVPCGTEKNFTNGMVNGH MPSLPDSPFTGYIIAVHRKM MRTELYFLSPQENRPSLFGM PLIVPCTVHTRKKDLYDAVW IQVSWLARPLPPQEASIHAQ DRDNCMGYQYPFTLRVVQKD GNSCAWCPQYRFCRGCKIDC GEDRAFIGNAYIAVDWHPTA LHLRYQTSQERVVDKHESVE QSRRAQAEPINLDSCLRAFT SEEELGESEMYYCSKCKTHC LATKKLDLWRLPPFLIIHLK RFQFVNDQWIKSQKIVRFLR ESFDPSAFLVPRDPALCQHK PLTPQGDELSKPRILAREVK KVDAQSSAGKEDMLLSKSPS SLSANISSSPKGSPSSSRKS GTSCPSSKNSSPNSSPRTLG

		RYGLRLNMDEKYTGLKKQLRDL CGLNSEQILLAEVHDSNIKNFP QDNQKVQLSVSGFLCAFEIPVP SSPISASSPTQIDFSSSPSTNG MFTLTTNGDLPKPIFIPNGMPN TVVPCGTEKNFTNGMVNGHMPS LPDSPFTGYIIAVHRKMMRTEL YFLSPQENRPSLFG MPLIVPCTVHTRKKDLYDAVWI QVSWLARPLPPQEASIHAQDRD NCMGYQYPFTLRVVQKDGNSCA WCPQYRFCRGCKIDCGEDRAFI GNAYIAVDWHPTALHLRYQTSQ ERVVDKHESVEQSRRAQAEPIN LDSCLRAFTSEEELGESEMYYC SKCKTHCLATKKLDLWRLPPFL IIHLKRFQFVNDQWIKSQKIVR FLRESFDPSAFLVPRDPALCQH KPLTPQGDELSKPRILAREVKK VDAQSSAGKEDMLLSKSPSSLS ANISSSPKGSPSSSRKSGTSCP SSKNSSPNSSPRTL GRSKGRLRLPQIGSKNKPSSSK KNLDASKENGAGQICELADALS RGHMRGGSQPELVTPQDHEVAL ANGFLYEHEACGNGCGDGYSNG QLGNHSEEDSTDDQREDTHIKP IYNLYAISCHSGILSGGHYITY AKNPNCKWYCYNDSSCEELHPD EIDTDSAYILFYEQQGIDYAQF LPKIDGKKMADTSSTDEDSESD YEKYSMLQ		RSKGRLRLPQIGSKNKPSSS KKNLDASKENGAGQICELAD ALSRGHMRGGSQPELVTPQD HEVALANGFLYEHEACGNGC GDGYSNGQLGNHSEEDSTDD QREDTHIKPIYNLYAISCHS GILSGGHYITYAKNPNCKWY CYNDSSCEELHPDEIDTDSA YILFYEQQG
UBP53_HUMAN Inactive ubiquitin carboxyl-terminal hydrolase 53	56	MAWVKFLRKPGGNLGKVYQPGS MLSLAPTKGLLNEPGQNSCFLN SAVQVLWQLDIFRRSLRVLTGH VCQGDACIFCALKTIFAQFQHS REKALPSDNIRHALAESFKDEQ RFQLGLMDDAAECFENMLERIH FHIVPSRDADMCTSKSCITHQK FAMTLYEQCVCRSCGASSDPLP FTEFVRYISTTALCNEVERMLE RHERFKPEMFAELLQAANTTDD YRKCPSNCGQKIKIRRVLMNCP EIVTIGLVWDSEHSDLTEAVVR NLATHLYLPGLFYRVTDENAKN SELNLVGMICYTSQ HYCAFAFHTKSSKWVFFDDANV KEIGTRWKDVVSKCIRCHFQPL LLFYANPDGTAVSTEDALRQVI SWSHYKSVAENMGCEKPVIHKS DNLKENGFGDQAKQRENQKFPT	168	APTKGLLNEPGQNSCFLNSA VQVLWQLDIFRRSLRVLTGH VCQGDACIFCALKTIFAQFQ HSREKALPSDNIRHALAESF KDEQRFQLGLMDDAAECFEN MLERIHFHIVPSRDADMCTS KSCITHQKFAMTLYEQCVCR SCGASSDPLPFTEFVRYIST TALCNEVERMLERHERFKPE MFAELLQAANTTDDYRKCPS NCGQKIKIRRVLMNCPEIVT IGLVWDSEHSDLTEAVVRNL ATHLYLPGLFYRVTDENAKN SELNLVGMICYTSQHYCAFA FHTKSSKWVFFDDANVKEIG TRWKDVVSKCIRCHFQPLLL FYANPDGTAVSTEDALRQVI SWSHYKSVAENMGCEKPVIH KSDNLKENGFGDQAKQRENQ

		DNISSSNRSHSHTGVGKGPAKL SHIDQREKIKDISRECALKAIE QKNLLSSQRKDLEKGQRKDLGR HRDLVDEDLSHFQSGSPPAPNG FKQHGNPHLYHSQGKGSYKHDR VVPQSRASAQIISSSKSQILAP GEKITGKVKSDNGTGYDTDSSQ DSRDRGNSCDSSSKSRNRGWKP MRETLNVDSIFSES EKRQHSPRHKPNISNKPKSSKD PSFSNWPKENPKQKGLMTIYED EMKQEIGSRSSLESNGKGAEKN KGLVEGKVHGDNWQMQRTESGY ESSDHISNGSTNLDSPVIDGNG TVMDISGVKETVCFSDQITTSN LNKERGDCTSLQSQHHLEGFRK ELRNLEAGYKSHEFHPESHLQI KNHLIKRSHVHEDNGKLFPSSS LQIPKDHNAREHIHQSDEQKLE KPNECKFSEWLNIENSERTGLP FHVDNSASGKRVNSNEPSSLWS SHLRTVGLKPETAPLIQQQNIM DQCYFENSLSTECI IRSASRSDGCQMPKLFCQNLPP PLPPKKYAITSVPQSEKSESTP DVKLTEVFKATSHLPKHSLSTA SEPSLEVSTHMNDERHKETFQV RECFGNTPNCPSSSSTNDFQAN SGAIDAFCQPELDSISTCPNET VSLTTYFSVDSCMTDTYRLKYH QRPKLSFPESSGFCNNSLS		KFPTDNISSSNRSHSHTGVG KGPAKLSHIDQREKIKDISR ECALKAIEQKNLLSSQRKDL EKGQRK
U17LO_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 24	57	MEDDSLYLRGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KTLTLHTSAKVLILVLKRFSDV TGNKIAKNVQYPEC LDMQPYMSQPNTGPLVYVLYAV LVHAGWSCHNGHYFSYVKAQEG QWYKMDDAEVTASSITSVLSQQ AYVLFYIQKSEWERHSESVSRG REPRALGAEDTDRRATQGELKR DHPCLQAPELDEHLVERATQES	169	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQPNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS

		TLDHWKFLQEQNKTKPEFNVRK VEGTLPPDVLVIHQSKYKCGMK NHHPEQQSSLLNLSSSTPTHQE SMNTGTLASLRGRARRSKGKNK HSKRALLVCQ		
U17LM_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 22		MEDDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KTLTLHTSAKVLILVLKRFSDV TGNKIAKNVQYPEC LDMQPYMSQQNTGPLVYVLYAV LVHAGWSCHNGHYFSYVKAQEG QWYKMDDAEVTASSITSVLSQQ AYVLFYIQKSEWERHSESVSRG REPRALGAEDTDRRATQGELKR DHPCLQAPELDEHLVERATQES TLDHWKFLQEQNKTKPEFNVRK VEGTLPPDVLVIHQSKYKCGMK NHHPEQQSSLLKLSSTTPTHQE SMNTGTLASLRGRARRSKGKNK HSKRALLVCQ		AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQQNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS
UBP5_HUMAN Ubiquitin carboxyl-terminal hydrolase 5	58	MAELSEEALLSVLPTIRVPKAG DRVHKDECAFSFDTPESEGGLY ICMNTFLGFGKQYVERHFNKTG QRVYLHLRRTRRPKEEDPATGT GDPPRKKPTRLAIGVEGGFDLS EEKFELDEDVKIVILPDYLEIA RDGLGGLPDIVRDRVTSAVEAL LSADSASRKQEVQAWDGEVRQV SKHAFSLKQLDNPARIPPCGWK CSKCDMRENLWLNLTDGSILCG RRYFDGSGGNNHAVEHYRETGY PLAVKLGTITPDGADVYSYDED DMVLDPSLAEHLSHFGIDMLKM QKTDKTMTELEIDM NQRIGEWELIQESGVPLKPLFG PGYTGIRNLGNSCYLNSVVQVL FSIPDFQRKYVDKLEKIFQNAP TDPTQDFSTQVAKLGHGLLSGE YSKPVPESGDGERVPEQKEVQD GIAPRMFKALIGKGHPEFSTNR QQDAQEFFLHLINMVERNCRSS	170	FGPGYTGIRNLGNSCYLNSV VQVLFSIPDFQRKYVDKLEK IFQNAPTDPTQDFSTQVAKL GHGLLSGEYSKPVPESGDGE RVPEQKEVQDGIAPRMFKAL IGKGHPEFSTNRQQDAQEFF LHLINMVERNCRSSENPNEV FRFLVEEKIKCLATEKVKYT QRVDYIMQLPVPMDAALNKE ELLEYEEKKRQAEEEKMALP ELVRAQVPFSSCLEAYGAPE QVDDFWSTALQAKSVAVKTT RFASFPDYLVIQIKKFTFGL DWVPKKLDVSIEMPEELDIS QLRGTGLQPGEEELPDIAPP LVTPDEPKGSLGFYGNEDED SFCSPHFSSPTSPMLDESVI IQLVEMGFPMDACRKAVYYT GNSGAEAAMNWVMSHMDDPD FANPLILPGSSGPGSTSAAA DPPPEDCVTTIVSMGFSRDQ

		ENPNEVFRFLVEEKIKCLATEK VKYTQRVDYIMQLPVPMDAALN KEELLEYEEKKRQAEEEKMALP ELVRAQVPFSSCLEAYGAPEQV DDFWSTALQAKSVAVKTTRFAS FPDYLVIQIKKFTFGLDWVPKK LDVSIEMPEELDIS QLRGTGLQPGEEELPDIAPPLV TPDEPKGSLGFYGNEDEDSFCS PHFSSPTSPMLDESVIIQLVEM GFPMDACRKAVYYTGNSGAEAA MNWVMSHMDDPDFANPLILPGS SGPGSTSAAADPPPEDCVTTIV SMGFSRDQALKALRATNNSLER AVDWIFSHIDDLDAEAAMDISE GRSAADSISESVPVGPKVRDGP GKYQLFAFISHMGTSTMCGHYV CHIKKEGRWVIYNDQKVCASEK PPKDLGYIYFYQRVAS		ALKALRATNNSLERAVDWIF SHIDDLDAEAAMDISEGRSA ADSISESVPVGPKVRDGPGK YQLFAFISHMGTSTMCGHYV CHIKKEGRWVIYNDQKVCAS EKPPKDLGYIYFYQRVA
UBP25_HUMAN Ubiquitin carboxyl-terminal hydrolase 25	59	MTVEQNVLQQSAAQKHQQTFLN QLREITGINDTQILQQALKDSN GNLELAVAFLTAKNAKTPQQEE TTYYQTALPGNDRYISVGSQAD TNVIDLTGDDKDDLQRAIALSL AESNRAFRETGITDEEQAISRV LEASIAENKACLKRTPTEVWRD SRNPYDRKRQDKAPVGLKNVGN TCWFSAVIQSLFNLLEFRRLVL NYKPPSNAQDLPRNQKEHRNLP FMRELRYLFALLVGTKRKYVDP SRAVEILKDAFKSNDSQQQDVS EFTHKLLDWLEDAFQMKAEEET DEEKPKNPMVELFY GRFLAVGVLEGKKFENTEMFGQ YPLQVNGFKDLHECLEAAMIEG EIESLHSENSGKSGQEHWFTEL PPVLTFELSRFEFNQALGRPEK IHNKLEFPQVLYLDRYMHRNRE ITRIKREEIKRLKDYLTVLQQR LERYLSYGSGPKRFPLVDVLQY ALEFASSKPVCTSPVDDIDASS PPSGSIPSQTLPSTTEQQGALS SELPSTSPSSVAAISSRSVIHK PFTQSRIPPDLPMHPAPRHITE EELSVLESCLHRWRTEIENDTR DLQESISRIHRTIELMYSDKSM IQVPYRLHAVLVHE GQANAGHYWAYIFDHRESRWMK YNDIAVTKSSWEELVRDSFGGY RNASAYCLMYINDKAQFLIQEE FNKETGQPLVGIETLPPDLRDF		KAPVGLKNVGNTCWFSAVIQ SLFNLLEFRRLVLNYKPPSN AQDLPRNQKEHRNLPFMREL RYLFALLVGTKRKYVDPSRA VEILKDAFKSNDSQQQDVSE FTHKLLDWLEDAFQMKAEEE TDEEKPKNPMVELFYGRFLA VGVLEGKKFENTEMFGQYPL QVNGFKDLHECLEAAMIEGE IESLHSENSGKSGQEHWFTE LPPVLTFELSRFEFNQALGR PEKIHNKLEFPQVLYLDRYM HRNREITRIKREEIKRLKDY LTVLQQRLERYLSYGSGPKR FPLVDVLQYALEFASSKPVC TSPVDDIDASSPPSGSIPSQ TLPSTTEQQGALSSELPSTS PSSVAAISSRSVIHKPFTQS RIPPDLPMHPAPRHITEEEL SVLESCLHRWRTEIENDTRD LQESISRIHRTIELMYSDKS MIQVPYRLHAVLVHEGQANA GHYWAYIFDHRESRWMKYND IAVTKSSWEELVRDSFGGYR NAS

		VEEDNQRFEKELEEWDAQLAQK ALQEKLLASQKLRESETSVTTA QAAGDPEYLEQPSRSDFSKHLK EETIQIITKASHEHEDKSPETV LQSAIKLEYARLVKLAQEDTPP ETDYRLHHVVVYFIQNQAPKKI IEKTLLEQFGDRNLSFDERCHN IMKVAQAKLEMIKPEEVNLEEY EEWHQDYRKFRETTMYLIIGLE NFQRESYIDSLLFL ICAYQNNKELLSKGLYRGHDEE LISHYRRECLLKLNEQAAELFE SGEDREVNNGLIIMNEFIVPFL PLLLVDEMEEKDILAVEDMRNR WCSYLGQEMEPHLQEKLTDFLP KLLDCSMEIKSFHEPPKLPSYS THELCERFARIMLSLSRTPADG R		
UBP33_HUMAN Ubiquitin carboxyl-terminal hydrolase 33	60	MTGSNSHITILTLKVLPHFESL GKQEKIPNKMSAFRNHCPHLDS VGEITKEDLIQKSLGTCQDCKV QGPNLWACLENRCSYVGCGESQ VDHSTIHSQETKHYLTVNLTTL RVWCYACSKEVFLDRKLGTQPS LPHVRQPHQIQENSVQDFKIPS NTTLKTPLVAVFDDLDIEADEE DELRARGLTGLKNIGNTCYMNA ALQALSNCPPLTQFFLDCGGLA RTDKKPAICKSYLKLMTELWHK SRPGSVVPTTLFQGIKTVNPTF RGYSQQDAQEFLRCLMDLLHEE LKEQVMEVEEDPQT ITTEETMEEDKSQSDVDFQSCE SCSNSDRAENENGSRCFSEDNN ETTMLIQDDENNSEMSKDWQKE KMCNKINKVNSEGEFDKDRDSI SETVDLNNQETVKVQIHSRASE YITDVHSNDLSTPQILPSNEGV NPRLSASPPKSGNLWPGLAPPH KKAQSASPKRKKQHKKYRSVIS DIFDGTIISSVQCLTCDRVSVT LETFQDLSLPIPGKEDLAKLHS SSHPTSIVKAGSCGEAYAPQGW IAFFMEYVKRFVVSCVPSWFWG PVVTLQDCLAAFFARDELKGDN MYSCEKCKKLRNGV KFCKVQNFPEILCIHLKRFRHE LMFSTKISTHVSFPLEGLDLQP FLAKDSPAQIVTYDLLSVICHH GTASSGHYIAYCRNNLNNLWYE FDDQSVTEVSESTVQNAEAYVL	171	ARGLTGLKNIGNTCYMNAAL QALSNCPPLTQFFLDCGGLA RTDKKPAICKSYLKLMTELW HKSRPGSVVPTTLFQGIKTV NPTFRGYSQQDAQEFLRCLM DLLHEELKEQVMEVEEDPQT ITTEETMEEDKSQSDVDFQS CESCSNSDRAENENGSRCFS EDNNETTMLIQDDENNSEMS KDWQKEKMCNKINKVNSEGE FDKDRDSISETVDLNNQETV KVQIHSRASEYITDVHSNDL STPQILPSNEGVNPRLSASP PKSGNLWPGLAPPHKKAQSA SPKRKKQHKKYRSVISDIFD GTIISSVQCLTCDRVSVTLE TFQDLSLPIPGKEDLAKLHS SSHPTSIVKAGSCGEAYAPQ GWIAFFMEYVKRFVVSCVPS WFWGPVVTLQDCLAAFFARD ELKGDNMYSCEKCKKLRNGV KFCKVQNFPEILCIHLKRFR HELMFSTKISTHVSFPLEGL DLQPFLAKDSPAQIVTYDLL SVICHHGTASSGHYIAYCRN NLNNLWYEFDDQSVTEVSES TVQNAEAYVLFYRKSS

		FYRKSSEEAQKERRRISNLLNI MEPSLLQFYISRQWLNKFKTFA EPGPISNNDFLCIHGGVPPRKA GYIEDLVLMLPQNIWDNLYSRY GGGPAVNHLYICHTCQIEAEKI EKRRKTELEIFIRLNRAFQKED SPATFYCISMQWFREWESFVKG KDGDPPGPIDNTKIAVTKCGNV MLRQGADSGQISEETWNFLQSI YGGGPEVILRPPVVHVDPDILQ AEEKIEVETRSL		
UBP21_HUMAN Ubiquitin carboxyl-terminal hydrolase 21	61	MPQASEHRLGRTREPPVNIQPR VGSKLPFAPRARSKERRNPASG PNPMLRPLPPRPGLPDERLKKL ELGRGRTSGPRPRGPLRADHGV PLPGSPPPTVALPLPSRTNLAR SKSVSSGDLRPMGIALGGHRGT GELGAALSRLALRPEPPTLRRS TSLRRLGGFPGPPTLFSIRTEP PASHGSFHMISARSSEPFYSDD KMAHHTLLLGSGHVGLRNLGNT CFLNAVLQCLSSTRPLRDFCLR RDFRQEVPGGGRAQELTEAFAD VIGALWHPDSCEAVNPTRFRAV FQKYVPSFSGYSQQ DAQEFLKLLMERLHLEINRRGR RAPPILANGPVPSPPRRGGALL EEPELSDDDRANLMWKRYLERE DSKIVDLFVGQLKSCLKCQACG YRSTTFEVFCDLSLPIPKKGFA GGKVSLRDCFNLFTKEEELESE NAPVCDRCRQKTRSTKKLTVQR FPRILVLHLNRFSASRGSIKKS SVGVDFPLQRLSLGDFASDKAG SPVYQLYALCNHSGSVHYGHYT ALCRCQTGWHVYNDSRVSPVSE NQVASSEGYVLFYQLMQEPPRC L	172	LGSGHVGLRNLGNTCFLNAV LQCLSSTRPLRDFCLRRDFR QEVPGGGRAQELTEAFADVI GALWHPDSCEAVNPTRFRAV FQKYVPSFSGYSQQDAQEFL KLLMERLHLEINRRGRRAPP ILANGPVPSPPRRGGALLEE PELSDDDRANLMWK RYLEREDSKIVDLFVGQLKS CLKCQACGYRSTTFEVFCDL SLPIPKKGFAGGKVSLRDCF NLFTKEEELESENAPVCDRC RQKTRSTKKLTVQRFPRILV LHLNRFSASRGSIKKSSVGV DFPLQRLSLGDFASDKAGSP VYQLYALCNHSGSVHYGHYT ALCRCQTGWHVYNDSRVSPV SENQVASSEGYVLFYQLMQ
U17L4_HUMAN Inactive ubiquitin carboxyl-terminal hydrolase 17-like protein 4	62	MGDDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS SETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYENASLQCLTYTLPLANYMLS REHSQTCQRPKCCMLCTMQAHI TWALHSPGHVIQPSQALAAGFH RGKQEDVHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GCWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVKQALEQLVK PEELNGENAYHCGLCLQRAPAS	173	AVGAGLQNMGNTCYENASLQ CLTYTLPLANYMLSREHSQT CQRPKCCMLCTMQAHITWAL HSPGHVIQPSQALAAGFHRG KQEDVHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGCWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVKQA LEQLVKPEELNGENAYHCGL CLQRAPASNTLTLHTSAKVL ILVLKRFSDVAGNKLAKNVQ YPECLDMQPYMSQQNTGPLV YVLYAVLVHAGWSCHDGYYF

		NTLTLHTSAKVLILVLKRFSDV AGNKLAKNVQYPEC LDMQPYMSQQNTGPLVYVLYAV LVHAGWSCHDGYYFSYVKAQEG QWYKMDDAEVTVCSITSVLSQQ AYVLFYIQKSEWERHSESVSRG REPRALGAEDTDRPATQGELKR DHPCLQVPELDEHLVERATEES TLDHWKFPQEQNKMKPEFNVRK VEGTLPPNVLVIHQSKYKCGMK NHHPEQQSSLLNLSSMNSTDQE SMNTGTLASLQGRTRRSKGKNK HSKRSLLVCQ		SYVKAQEGQWYKMDDAEVTV CSITSVLSQQAYVLFYIQKS
U17LK_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 20	63	MEDDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE KLPLSSRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KTLTLHTSAKVLILVLKRFSDV TGNKIAKNVQYPECLDMQPYMS QPNTGPLVYVLYAVLVHAGWSC HNGHYFSYVKAQEGQWYKMDDA EVTASSITSVLSQQAYVLFYIQ KSEWERHSESVSRGREPRALGA EDTDRRATQGELKRDHPCLQAP ELDEHLVERATQESTLDHWKFL QEQNKTKPEFNVRKVEGTLPPD VLVIHQSKYKCGMKNHHPEQQS SLLNLSSTTPTHQESMNTGTLA SLRGRARRSKGKNKHSKRALLV CQ	174	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKTLTLHTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQPNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS
UBP12_HUMAN Ubiquitin carboxyl-terminal hydrolase 12	64	MEILMTVSKFASICTMGANASA LEKEIGPEQFPVNEHYFGLVNF GNTCYCNSVLQALYFCRPFREK VLAYKSQPRKKESLLTCLADLF HSIATQKKKVGVIPPKKFITRL RKENELFDNYMQQDAHEFLNYL LNTIADILQEERKQEKQNGRLP NGNIDNENNNSTPDPTWVHEIF QGTLTNETRCLTCETISSKDED FLDLSVDVEQNTSITHCLRGFS NTETLCSEYKYYCEECRSKQEA HKRMKVKKLPMILALHLKRFKY	175	EHYFGLVNFGNTCYCNSVLQ ALYFCRPFREKVLAYKSQPR KKESLLTCLADLFHSIATQK KKVGVIPPKKFITRLRKENE LFDNYMQQDAHEFLNYLLNT IADILQEERKQEKQNGRLPN GNIDNENNNSTPDPTWVHEI FQGTLTNETRCLTCETISSK DEDFLDLSVDVEQNTSITHC LRGFSNTETLCSEYKYYCEE CRSKQEAHKRMKVKKLPMIL ALHLKRFKYMDQLHRYTKLS YRVVFPLELRLFNTSGDATN

		MDQLHRYTKLSYRVVFPLELRL FNTSGDATNPDRMY DLVAVVVHCGSGPNRGHYIAIV KSHDFWLLFDDDIVEKIDAQAI EEFYGLTSDISKNSESGYILFY QSRD		PDRMYDLVAVVVHCGSGPNR GHYIAIVKSHDFWLLFDDDI VEKIDAQAIEEFYGLTSDIS KNSESGYILFYQSR
UL17C_HUMAN Ubiquitin carboxyl-terminal hydrolase 17-like protein 12	65	MEEDSLYLGGEWQFNHFSKLTS SRPDAAFAEIQRTSLPEKSPLS CETRVDLCDDLAPVARQLAPRE KLPLSNRRPAAVGAGLQNMGNT CYVNASLQCLTYTPPLANYMLS REHSQTCHRHKGCMLCTMQAHI TRALHNPGHVIQPSQALAAGFH RGKQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQIFG GYWRSQIKCLHCHGISDTFDPY LDIALDIQAAQSVQQALEQLVK PEELNGENAYHCGVCLQRAPAS KMLTLLTSAKVLILVLKRFSDV TGNKIAKNVQYPEC LDMQPYMSQPNTGPLVYVLYAV LVHAGWSCHNGHYFSYVKAQEG QWYKMDDAEVTASSITSVLSQQ AYVLFYIQKSEWERHSESVSRG REPRALGAEDTDRRATQGELKR DHPCLQAPELDEHLVERATQES TLDHWKFLQEQNKTKPEFNVRK VEGTLPPDVLVIHQSKYKCGMK NHHPEQQSSLLKLSSTTPTHQE SMNTGTLASLRGRARRSKGKNK HSKRALLVCQ	176	AVGAGLQNMGNTCYVNASLQ CLTYTPPLANYMLSREHSQT CHRHKGCMLCTMQAHITRAL HNPGHVIQPSQALAAGFHRG KQEDAHEFLMFTVDAMKKAC LPGHKQVDHHSKDTTLIHQI FGGYWRSQIKCLHCHGISDT FDPYLDIALDIQAAQSVQQA LEQLVKPEELNGENAYHCGV CLQRAPASKMLTLLTSAKVL ILVLKRFSDVTGNKIAKNVQ YPECLDMQPYMSQPNTGPLV YVLYAVLVHAGWSCHNGHYF SYVKAQEGQWYKMDDAEVTA SSITSVLSQQAYVLFYIQKS
UBP20_HUMAN Ubiquitin carboxyl-terminal hydrolase	66	MGDSRDLCPHLDSIGEVTKEDL LLKSKGTCQSCGVTGPNLWACL QVACPYVGCGESFADHSTIHAQ AKKHNLTVNLTTFRLWCYACEK EVFLEQRLAAPLLGSSSKFSEQ DSPPPSHPLKAVPIAVADEGES ESEDDDLKPRGLTGMKNLGNSC YMNAALQALSNCPPLTQFFLEC GGLVRTDKKPALCKSYQKLVSE VWHKKRPSYVVPTSLSHGIKLV NPMFRGYAQQDTQEFLRCLMDQ LHEELKEPVVATVALTEARDSD SSDTDEKREGDRSPSEDEFLSC DSSSDRGEGDGQGR GGGSSQAETELLIPDEAGRAIS EKERMKDRKFSWGQQRTNSEQV DEDADVDTAMAALDDQPAEAQP PSPRSSSPCRTPEPDNDAHLRS SSRPCSPVHHHEGHAKLSSSPP RASPVRMAPSYVLKKAQVLSAG	177	PRGLTGMKNLGNSCYMNAAL QALSNCPPLTQFFLECGGLV RTDKKPALCKSYQKLVSEVW HKKRPSYVVPTSLSHGIKLV NPMFRGYAQQDTQEFLRCLM DQLHEELKEPVVATVALTEA RDSDSSDTDEKREGDRSPSE DEFLSCDSSSDRGEGDGQGR GGGSSQAETELLIPDEAGRA ISEKERMKDRKFSWGQQRTN SEQVDEDADVDTAMAALDDQ PAEAQPPSPRSSSPCRTPEP DNDAHLRSSSRPCSPVHHHE GHAKLSSSPPRASPVRMAPS YVLKKAQVLSAGSRRRKEQR YRSVISDIFDGSILSLVQCL TCDRVSTTVETFQDLSLPIP GKEDLAKLHSAIYQNVPAKP GACGDSYAAQGWLAFIVEYI RRFVVSCTPSWFWGPVVTLE

		SRRRKEQRYRSVISDIFDGSIL SLVQCLTCDRVSTTVETFQDLS LPIPGKEDLAKLHSAIYQNVPA KPGACGDSYAAQGWLAFIVEYI RRFVVSCTPSWFWGPVVTLEDC LAAFFAADELKGDNMYSCERCK KLRNGVKYCKVLRLPEILCIHL KRFRHEVMYSFKIN SHVSFPLEGLDLRPFLAKECTS QITTYDLLSVICHHGTAGSGHY IAYCQNVINGQWYEFDDQYVTE VHETVVQNAEGYVLFYRKSSEE AMRERQQVVSLAAMREPSLLRF YVSREWLNKFNTFAEPGPITNQ TFLCSHGGIPPHKYHYIDDLVV ILPQNVWEHLYNRFGGGPAVNH LYVCSICQVEIEALAKRRRIEI DTFIKLNKAFQAEESPGVIYCI SMQWFREWEAFVKGKDNEPPGP IDNSRIAQVKGSGHVQLKQGAD YGQISEETWTYLNSLYGGGPEI AIRQSVAQPLGPENLHGEQKIE AETRAV		DCLAAFFAADELKGDNMYSC ERCKKLRNGVKYCKVLRLPE ILCIHLKRFRHEVMYSFKIN SHVSFPLEGLDLRPFLAKEC TSQITTYDLLSVICHHGTAG SGHYIAYCQNVINGQWYEFD DQYVTEVHETVVQNAEGYVL FYRKSS
UBP46_HUMAN Ubiquitin carboxyl-terminal hydrolase 46	67	MTVRNIASICNMGTNASALEKD IGPEQFPINEHYFGLVNFGNTC YCNSVLQALYFCRPFRENVLAY KAQQKKKENLLTCLADLFHSIA TQKKKVGVIPPKKFISRLRKEN DLFDNYMQQDAHEFLNYLLNTI ADILQEEKKQEKQNGKLKNGNM NEPAENNKPELTWVHEIFQGTL TNETRCLNCETVSSKDEDFLDL SVDVEQNTSITHCLRDFSNTET LCSEQKYYCETCCSKQEAQKRM RVKKLPMILALHLKRFKYMEQL HRYTKLSYRVVFPLELRLFNTS SDAVNLDRMYDLVA VVVHCGSGPNRGHYITIVKSHG FWLLFDDDIVEKIDAQAIEEFY GLTSDISKNSESGYILFYQSRE	178	EHYFGLVNFGNTCYCNSVLQ ALYFCRPFRENVLAYKAQQK KKENLLTCLADLFHSIATQK KKVGVIPPKKFISRLRKEND LFDNYMQQDAHEFLNYLLNT IADILQEEKKQEKQNGKLKN GNMNEPAENNKPELTWVHEI FQGTLTNETRCLNCETVSSK DEDFLDLSVDVEQNTSITHC LRDFSNTETLCSEQKYYCET CCSKQEAQKRMRVKKLPMIL ALHLKRFKYMEQLHRYTKLS YRVVFPLELRLFNTSSDAVN LDRMYDLVAVVVHCGSGPNR GHYITIVKSHGFWLLFDDDI VEKIDAQAIEEFYGLTSDIS KNSESGYILFYQSR
CYLD_HUMAN Ubiquitin carboxyl-terminal hydrolase CYLD	68	MSSGLWSQEKVTSPYWEERIFY LLLQECSVTDKQTQKLLKVPKG SIGQYIQDRSVGHSRIPSAKGK KNQIGLKILEQPHAVLFVDEKD VVEINEKFTELLLAITNCEERF SLFKNRNRLSKGLQIDVGCPVK VQLRSGEEKFPGVVRFRGPLLA ERTVSGIFFGVELLEEGRGQGF TDGVYQGKQLFQCDEDCGVFVA LDKLELIEDDDTALESDYAGPG DTMQVELPPLEINSRVSLKVGE	179	GKKKGIQGHYNSCYLDSTLF CLFAFSSVLDTVLLRPKEKN DVEYYSETQELLRTEIVNPL RIYGYVCATKIMKLRKILEK VEAASGFTSEEKDPEEFLNI LFHHILRVEPLLKIRSAGQK VQDCYFYQIFME KNEKVGVPTIQQLLEWSFIN SNLKFAEAPSCLIIQMPRFG KDFKLFKKIFPSLELNITDL LEDTPRQCRICGGLAMYECR

		TIESGTVIFCDVLPGKESLGYF VGVDMDNPIGNWDGRFDGVQLC SFACVESTILLHIN DIIPALSESVTQERRPPKLAFM SRGVGDKGSSSHNKPKATGSTS DPGNRNRSELFYTLNGSSVDSQ PQSKSKNTWYIDEVAEDPAKSL TEISTDFDRSSPPLQPPPVNSL TTENRFHSLPFSLTKMPNTNGS IGHSPLSLSAQSVMEELNTAPV QESPPLAMPPGNSHGLEVGSLA EVKENPPFYGVIRWIGQPPGLN EVLAGLELEDECAGCTDGTFRG TRYFTCALKKALFVKLKSCRPD SRFASLQPVSNQIERCNSLAFG GYLSEVVEENTPPKMEKEGLEI MIGKKKGIQGHYNS CYLDSTLFCLFAFSSVLDTVLL RPKEKNDVEYYSETQELLRTEI VNPLRIYGYVCATKIMKLRKIL EKVEAASGFTSEEKDPEEFLNI LFHHILRVEPLLKIRSAGQKVQ DCYFYQIFMEKNEKVGVPTIQQ LLEWSFINSNLKFAEAPSCLII QMPRFGKDFKLFKKIFPSLELN ITDLLEDTPRQCRICGGLAMYE CRECYDDPDISAGKIKQFCKTC NTQVHLHPKRLNHKYNPVSLPK DLPDWDWRHGCIPCQNMELFAV LCIETSHYVAFVKYGKDDSAWL FFDSMADRDGGQNGFNIPQVTP CPEVGEYLKMSLEDLHSLDSRR IQGCARRLLCDAYMCMYQSPTM SLYK		ECYDDPDISAGKIKQFCKTC NTQVHLHPKRLNHKYNPVSL PKDLPDWDWRHGCIPCQNME LFAVLCIETSHYVAFVKYGK DDSAWLFFDSMADRDGGQNG FNIPQVTPCPEVGEYLKMSL EDLHSLDSRRIQGCARRLLC DAYMCMYQSPT
UBP16_HUMAN Ubiquitin carboxyl-terminal hydrolase 16	69	MGKKRTKGKTVPIDDSSETLEP VCRHIRKGLEQGNLKKALVNVE WNICQDCKTDNKVKDKAEEETE EKPSVWLCLKCGHQGCGRNSQE QHALKHYLTPRSEPHCLVLSLD NWSVWCYVCDNEVQYCSSNQLG QVVDYVRKQASITTPKPAEKDN GNIELENKKLEKESKNEQEREK KENMAKENPPMNSPCQITVKGL SNLGNTCFFNAVMQNLSQTPVL RELLKEVKMSGTIVKIEPPDLA LTEPLEINLEPPGPLTLAMSQF LNEMQETKKGVVTPKELFSQVC KKAVRFKGYQQQDS QELLRYLLDGMRAEEHQRVSKG ILKAFGNSTEKLDEELKNKVKD YEKKKSMPSFVDRIFGGELTSM	180	ITVKGLSNLGNTCFFNAVMQ NLSQTPVLRELLKEVKMSGT IVKIEPPDLALTEPLEINLE PPGPLTLAMSQFLNEMQETK KGVVTPKELFSQVCKKAVRF KGYQQQDSQELLRYLLDGMR AEEHQRVSKGILKAFGNSTE KLDEELKNKVKDYEKKKSMP SFVDRIFGGELTSMIMCDQC RTVSLVHESFLDLSLPVLDD QSGKKSVNDKNLKKTVEDED QDSEEEKDNDSYIKERSDIP SGTSKHLQKKAKKQAKKQAK NQRRQQKIQGKVLHLNDICT IDHPEDSEYEAEMSLQGEVN IKSNHISQEGVMHKEYCVNQ KDLNGQAKMIESVTDNQKST

		IMCDQCRTVSLVHESFLDLSLP VLDDQSGKKSVNDKNLKKTVED EDQDSEEEKDNDSYIKERSDIP SGTSKHLQKKAKKQAKKQAKNQ RRQQKIQGKVLHLNDICTIDHP EDSEYEAEMSLQGEVNIKSNHI SQEGVMHKEYCVNQKDLNGQAK MIESVTDNQKSTEEVDMKNINM DNDLEVLTSSPTRNLNGAYLTE GSNGEVDISNGFKNLNLNAALH PDEINIEILNDSHT PGTKVYEVVNEDPETAFCTLAN REVFNTDECSIQHCLYQFTRNE KLRDANKLLCEVCTRRQCNGPK ANIKGERKHVYTNAKKQMLISL APPVLTLHLKRFQQAGFNLRKV NKHIKFPEILDLAPFCTLKCKN VAEENTRVLYSLYGVVEHSGTM RSGHYTAYAKARTANSHLSNLV LHGDIPQDFEMESKGQWFHISD THVQAVPTTKVLNSQAYLLFYE RIL		EEVDMKNINMDNDLEVLTSS PTRNLNGAYLTEGSNGEVDI SNGFKNLNLNAALHPDEINI EILNDSHTPGTKVYEVVNED PETAFCTLANREVFNTDECS IQHCLYQFTRNEKLRDANKL LCEVCTRRQCNGPKANIKGE RKHVYTNAKKQMLISLAPPV LTLHLKRFQQAGFNLRKVNK HIKFPEIL DLAPFCTLKCKNVAEENTRV LYSLYGVVEHSGTMRSGHYT AYAKARTANSHLSNLVLHGD IPQDFEMESKGQWFHISDTH VQAVPTTKVLNSQAYLLFYE RIL
ALG13_HUMAN Putative bifunctional UDP-N-acetylglucosamine transferase and deubiquitinase ALG13	70	MKCVFVTVGTTSFDDLIACVSA PDSLQKIESLGYNRLILQIGRG TVVPEPFSTESFTLDVYRYKDS LKEDIQKADLVISHAGAGSCLE TLEKGKPLVVVINEKLMNNHQL ELAKQLHKEGHLFYCTCRVLTC PGQAKSIASAPGKCQDSAALTS TAFSGLDFGLLSGYLHKQALVT ATHPTCTLLFPSCHAFFPLPLT PTLYKMHKGWKNYCSQKSLNEA SMDEYLGSLGLFRKLTAKDASC LFRAISEQLFCSQVHHLEIRKA CVSYMRENQQTFESYVEGSFEK YLERLGDPKESAGQ LEIRALSLIYNRDFILYRFPGK PPTYVTDNGYEDKILLCYSSSG HYDSVYSKQFQSSAAVCQAVLY EILYKDVFVVDEEELKTAIKLF RSGSKKNRNNAVTGSEDAHTDY KSSNQNRMEEWGACYNAENIPE GYNKGTEETKSPENPSKMPFPY KVLKALDPEIYRNVEFDVWLDS RKELQKSDYMEYAGRQYYLGDK CQVCLESEGRYYNAHIQEVGNE NNSVTVFIEELAEKHVVPLANL KPVTQVMSVPAWNAMPSRKGRG YQKMPGGYVPEIVISEMDIKQQ KKMFKKIRGKEVYM	181	YRYKDSLKEDIQKADLVISH AGAGSCLETLEKGKPLVVVI NEKLMNNHQLELAKQLHKEG HLFYCTCRVLTCPGQAKSIA SAPGKCQDSAALTSTAFSGL DFGLLSGYLHKQALVTATHP TCTLLFPSCHAFFPLPLTPT LYKMHKGWKNYCSQKSLNEA SMDEYLGSLGLFRKLTAKDA SCLFRAISEQLFCSQVHHLE IRKACVSYMRENQQTFESYV EGSFEKYLERLGDPKESAGQ LEIRALSLIYNRDFILYRFP GKPPTYVTDNGYEDKILLCY SSSGHYDSVYS

		TMAYGKGDPLLPPRLQHSMHYG HDPPMHYSQTAGNVMSNEHFHP QHPSPRQGRGYGMPRNSSRFIN RHNMPGPKVDFYPGPGKRCCQS YDNFSYRSRSFRRSHRQMSCVN KESQYGFTPGNGQMPRGLEETI TFYEVEEGDETAYPTLPNHGGP STMVPATSGYCVGRRGHSSGKQ TLNLEEGNGQSENGRYHEEYLY RAEPDYETSGVYSTTASTANLS LQDRKSCSMSPQDTVTSYNYPQ KMMGNIAAVAASCANNVPAPVL SNGAAANQAISTTSVSSQNAIQ PLFVSPPTHGRPVI ASPSYPCHSAIPHAGASLPPPP PPPPPPPPPPPPPPPPPPPPP PALDVGETSNLQPPPPLPPPPY SCDPSGSDLPQDTKVLQYYFNL GLQCYYHSYWHSMVYVPQMQQQ LHVENYPVYTEPPLVDQTVPQC YSEVRREDGIQAEASANDTFPN ADSSSVPHGAVYYPVMSDPYGQ PPLPGFDSCLPVVPDYSCVPPW HPVGTAYGGSSQIHGAINPGPI GCIAPSPPASHYVPQGM		
OTU1_HUMAN Ubiquitin thioesterase OTU1	71	MFGPAKGRHFGVHPAPGFPGGV SQQAAGTKAGPAGAWPVGSRTD TMWRLRCKAKDGTHVLQGLSSR TRVRELQGQIAAITGIAPGGQR ILVGYPPECLDLSNGDTILEDL PIQSGDMLIIEEDQTRPRSSPA FTKRGASSYVRETLPVLTRTVV PADNSCLFTSVYYVVEGGVLNP ACAPEMRRLIAQIVASDPDFYS EAILGKTNQEYCDWIKRDDTWG GAIEISILSKFYQCEICVVDTQ TVRIDRFGEDAGYTKRVLLIYD GIHYDPLQRNFPDPDTPPLTIF SSNDDIVLVQALELADEARRRR QFTDVNRFTLRCMVCQKGLTGQ AEAREHAKETGHTNFGEV	182	QGLSSRTRVRELQGQIAAIT GIAPGGQRILVGYPPECLDL SNGDTILEDLPIQSGDMLII EEDQTRPRSSPAFTKRGASS YVRETLPVLTRTVVPADNSC LFTSVYYVVEGGVLNPACAP EMRRLIAQIVASDPDFYSEA ILGKTNQEYCDWIKRDDTWG GAIEISILSKFYQCEICVVD TQTVRIDRFGEDAGYTKRVL LIYDGIHYDPLQ
OTUD1_HUMAN OTU domain-containing protein 1	72	MQLYSSVCTHYPAGAPGPTAAA PAPPAAATPFKVSLQPPGAAGA APEPETGECQPAAAAEHREAAA VPAAKMPAFSSCFEVVSGAAAP ASAAAGPPGASCKPPLPPHYTS TAQITVRALGADRLLLHGPDPV PGAAGSAAAPRGRCLLLAPAPA APVPPRRGSSAWLLEELLRPDC PEPAGLDATREGPDRNFRLSEH RQALAAAKHRGPAATPGSPDPG	183	HREAAAVPAAKMPAFSSCFE VVSGAAAPASAAAGPPGASC KPPLPPHYTSTAQITVRALG ADRLLLHGPDPVPGAAGSAA APRGRCLLLAPAPAAPVPPR RGSSAWLLEELLRPDCPEPA GLDATREGPDRNFRLSEHRQ ALAAAKHRGPAATPGSPDPG PGPWGEEHLAERGPRGWERG GDRCDAPGGDAARRPDPEAE

		PGPWGEEHLAERGPRGWERGGD RCDAPGGDAARRPDPEAEAPPA GSIEAAPSSAAEPVIVSRSDPR DEKLALYLAEVEKQ DKYLRQRNKYRFHIIPDGNCLY RAVSKTVYGDQSLHRELREQTV HYIADHLDHFSPLIEGDVGEFI IAAAQDGAWAGYPELLAMGQML NVNIHLTTGGRLESPTVSTMIH YLGPEDSLRPSIWLSWLSNGHY DAVFDHSYPNPEYDNWCKQTQV QRKRDEELAKSMAISLSKMYIE QNACS		APPAGSIEAAPSSAAEPVIV SRSDPRDEKLALYLAEVEKQ DKYLRQRNKYRFHIIPDGNC LYRAVSKTVYGDQSLHRELR EQTVHYIADHLDHFSPLIEG DVGEFIIAAAQDGAWAGYPE LLAMGQMLNVNIHLTTGGRL ESPTVSTMIHYLGPEDSLRP SIWLSWLSNGHYDAV
OTU6B_HUMAN Deubiquitinase OTUD6B	73	MEAVLTEELDEEEQLLRRHRKE KKELQAKIQGMKNAVPKNDKKR RKQLTEDVAKLEKEMEQKHREE LEQLKLTTKENKIDSVAVNISN LVLENQPPRISKAQKRREKKAA LEKEREERIAEAEIENLTGARH MESEKLAQILAARQLEIKQIPS DGHCMYKAIEDQLKEKDCALTV VALRSQTAEYMQSHVEDFLPFL TNPNTGDMYTPEEFQKYCEDIV NTAAWGGQLELRALSHILQTPI EIIQADSPPIIVGEEYSKKPLI LVYMRHAYGLGEHYNSVTRLVN IVTENCS	184	QKHREELEQLKLTTKENKID SVAVNISNLVLENQPPRISK AQKRREKKAALEKEREERIA EAEIENLTGARHMESEKLAQ ILAARQLEIKQIPSDGHCMY KAIEDQLKEKDCALTVVALR SQTAEYMQSHVEDFLPFLTN PNTGDMYTPEEFQKYCEDIV NTAAWGGQLELRALSHILQT PIEIIQADSPPIIVGEEYSK KPLILVYMRHAYG
OTU6A_HUMAN OTU domain-containing protein 6A	74	MDDPKSEQQRILRRHQRERQEL QAQIRSLKNSVPKTDKTKRKQL LQDVARMEAEMAQKHRQELEKF QDDSSIESVVEDLAKMNLENRP PRSSKAHRKRERMESEERERQE SIFQAEMSEHLAGFKREEEEKL AAILGARGLEMKAIPADGHCMY RAIQDQLVFSVSVEMLRCRTAS YMKKHVDEFLPFFSNPETSDSF GYDDFMIYCDNIVRTTAWGGQL ELRALSHVLKTPIEVIQADSPT LIIGEEYVKKPIILVYLRYAYS LGEHYNSVTPLEAGAAGGVLPR LL	185	QELEKFQDDSSIESVVEDLA KMNLENRPPRSSKAHRKRER MESEERERQESIFQAEMSEH LAGFKREEEEKLAAILGARG LEMKAIPADGHCMYRAIQDQ LVFSVSVEMLRCRTASYMKK HVDEFLPFFSNPETSDSFGY DDFMIYCDNIVRTTAWGGQL ELRALSHVLKTPIEVIQADS PTLIIGEEYVKKPIILVYLR YAYS
OTUB1_HUMAN Ubiquitin thioesterase OTUB1	75	MAAEEPQQQKQEPLGSDSEGVN CLAYDEAIMAQQDRIQQEIAVQ NPLVSERLELSVLYKEYAEDDN IYQQKIKDLHKKYSYIRKTRPD GNCFYRAFGFSHLEALLDDSKE LQRFKAVSAKSKEDLVSQGFTE FTIEDFHNTFMDLIEQVEKQTS VADLLASFNDQSTSDYLVVYLR LLTSGYLQRESKFFEHFIEGGR TVKEFCQQEVEPMCKESDHIHI	75	MAAEEPQQQKQEPLGSDSEG VNCLAYDEAIMAQQDRIQQE IAVQNPLVSERLELSVLYKE YAEDDNIYQQKIKDLHKKYS YIRKTRPDGNCFYRAFGFSH LEALLDDSKELQRFKAVSAK SKEDLVSQGFTEFTIEDFHN TFMDLIEQVEKQTSVADLLA SFNDQSTSDYLVVYLRLLTS GYLQRESKFFEHFIEGGRTV

		IALAQALSVSIQVEYMDRGEGG TTNPHIFPEGSEPKVYLLYRPG HYDILYK		KEFCQQEVEPMCKESDHIHI IALAQALSVSIQVEYMDRGE GGTTNPHIFPEGSEPKVYLL YRPGHYDILYK
OTU7A_HUMAN OTU domain-containing protein 7A	76	MVSSVLPNPTSAECWAALLHDP MTLDMDAVLSDFVRSTGAEPGL ARDLLEGKNWDLTAALSDYEQL RQVHTANLPHVFNEGRGPKQPE REPQPGHKVERPCLQRQDDIAQ EKRLSRGISHASSAIVSLARSH VASECNNEQFPLEMPIYTFQLP DLSVYSEDFRSFIERDLIEQAT MVALEQAGRLNWWSTVCTSCKR LLPLATTGDGNCLLHAASLGMW GFHDRDLVLRKALYTMMRTGAE REALKRRWRWQQTQQNKEEEWE REWTELLKLASSEPRTHFSKNG GTGGGVDNSEDPVY ESLEEFHVFVLAHILRRPIVVV ADTMLRDSGGEAFAPIPFGGIY LPLEVPPNRCHCSPLVLAYDQA HFSALVSMEQRDQQREQAVIPL TDSEHKLLPLHFAVDPGKDWEW GKDDNDNARLAHLILSLEAKLN LLHSYMNVTWIRIPSETRAPLA QPESPTASAGEDVQSLADSLDS DRDSVCSNSNSNNGKNGKDKEK EKQRKEKDKTRADSVANKLGSF SKTLGIKLKKNMGGLGGLVHGK MGRANSANGKNGDSAERGKEKK AKSRKGSKEESGASASTSPSEK TTPSPTDKAAGASP AEKGGGPRGDAWKYSTDVKLSL NILRAAMQGERKFIFAGLLLTS HRHQFHEEMIGYYLTSAQERFS AEQEQRRRDAATAAAAAAAAAA ATAKRPPRRPETEGVPVPERAS PGPPTQLVLKLKERPSPGPAAG RAARAAAGGTASPGGGARRASA SGPVPGRSPPAPARQSVIHVQA SGARDEACAPAVGALRPCATYP QQNRSLSSQSYSPARAAALRTV NTVESLARAVPGALPGAAGTAG AAEHKSQTYTNGFGALRDGLEF ADADAPTARSNGECGRGGPGPV QRRCQRENCAFYGRAETEHYCS YCYREELRRRREARGARP	186	SDYEQLRQVHTANLPHVFNE GRGPKQPEREPQPGHKVERP CLQRQDDIAQEKRLSRGISH ASSAIVSLARSHVASECNNE QFPLEMPIYTFQLPDLSVYS EDFRSFIERDLIEQATMVAL EQAGRLNWWSTVCTSCKRLL PLATTGDGNCLLHAASLGMW GFHDRDLVLRKALYTMMRTG AEREALKRRWRWQQTQQNKE EEWEREWTELLKLASSEPRT HFSKNGGTGGGVDNSEDPVY ESLEEFHVFVLAHILRRPIV VVADTMLRDSGGEAFAPIPF GGIYLPLEVPPNRCHCSPLV LAYDQAHFSAL
OTUD4_HUMAN OTU domain-	77	MEAAVGVPDGGDQGGAGPREDA TPMDAYLRKLGLYRKLVAKDGS CLFRAVAEQVLHSQSRHVEVRM ACIHYLRENREKFEAFIEGSFE	187	MEAAVGVPDGGDQGGAGPRE DATPMDAYLRKLGLYRKLVA KDGSCLFRAVAEQVLHSQSR HVEVRMACIHYLRENREKFE

containing protein 4		EYLKRLENPQEWVGQVEISALS LMYRKDFIIYREPNVSPSQVTE NNFPEKVLLCFSNGNHYDIVYP IKYKESSAMCQSLLYELLYEKV FKTDVSKIVMELDTLEVADEDN SEISDSEDDSCKSKTAAAAADV NGFKPLSGNEQLKNNGNSTSLP LSRKVLKSLNPAVYRNVEYEIW LKSKQAQQKRDYSIAAGLQYEV GDKCQVRLDHNGKF LNADVQGIHSENGPVLVEELGK KHTSKNLKAPPPESWNTVSGKK MKKPSTSGQNFHSDVDYRGPKN PSKPIKAPSALPPRLQHPSGVR QHAFSSHSSGSQSQKFSSEHKN LSRTPSQIIRKPDRERVEDFDH TSRESNYFGLSPEERREKQAIE ESRLLYEIQNRDEQAFPALSSS SVNQSASQSSNPCVQRKSSHVG DRKGSRRRMDTEERKDKDSIHG HSQLDKRPEPSTLENITDDKYA TVSSPSKSKKLECPSPAEQKPA EHVSLSNPAPLLVSPEVHLTPA VPSLPATVPAWPSE PTTFGPTGVPAPIPVLSVTQTL TTGPDSAVSQAHLTPSPVPVSI QAVNQPLMPLPQTLSLYQDPLY PGFPCNEKGDRAIVPPYSLCQT GEDLPKDKNILRFFFNLGVKAY SCPMWAPHSYLYPLHQAYLAAC RMYPKVPVPVYPHNPWFQEAPA AQNESDCTCTDAHFPMQTEASV NGQMPQPEIGPPTFSSPLVIPP SQVSESHGQLSYQADLESETPG QLLHADYEESLSGKNMFPQSFG PNPFLGPVPIAPPFFPHVWYGY PFQGFIENPVMRQNIVLPSDEK GELDLSLENLDLS KDCGSVSTVDEFPEARGEHVHS LPEASVSSKPDEGRTEQSSQTR KADTALASIPPVAEGKAHPPTQ ILNRERETVPVELEPKRTIQSL KEKTEKVKDPKTAADVVSPGAN SVDSRVQRPKEESSEDENEVSN ILRSGRSKQFYNQTYGSRKYKS DWGYSGRGGYQHVRSEESWKGQ PSRSRDEGYQYHRNVRGRPFRG DRRRSGMGDGHRGQHT		AFIEGSFEEYLKRLENPQEW VGQVEISALSLMYRKDFIIY REPNVSPSQVTENNFPEKVL LCFSNGNHYDIVYP
OTUB2_HUMAN Ubiquitin	78	MSETSFNLISEKCDILSILRDH PENRIYRRKIEELSKRFTAIRK TKGDGNCFYRALGYSYLESLLG	78	MSETSFNLISEKCDILSILR DHPENRIYRRKIEELSKRFT AIRKTKGDGNCFYRALGYSY

thioesterase OTUB2		KSREIFKFKERVLQTPNDLLAA GFEEHKFRNFFNAFYSVVELVE KDGSVSSLLKVFNDQSASDHIV QFLRLLTSAFIRNRADFFRHFI DEEMDIKDFCTHEVEPMATECD HIQITALSQALSIALQVEYVDE MDTALNHHVFPEAATPSVYLLY KTSHYNILYAADKH		LESLLGKSREIFKFKERVLQ TPNDLLAAGFEEHKFRNFFN AFYSVVELVEKDGSVSSLLK VFNDQSASDHIVQFLRLLTS AFIRNRADFFRHFIDEEMDI KDFCTHEVEPMATECDHIQI TALSQALSIALQVEYVDEMD TALNHHVFPEAATPSVYLLY KTSHYNILYAADKH
OTUD3_HUMAN OTU domain-containing protein 3	79	MSRKQAAKSRPGSGSRKAEAER KRDERAARRALAKERRNRPESG GGGGCEEEFVSFANQLQALGLK LREVPGDGNCLFRALGDQLEGH SRNHLKHRQETVDYMIKQREDF EPFVEDDIPFEKHVASLAKPGT FAGNDAIVAFARNHQLNVVIHQ LNAPLWQIRGTEKSSVRELHIA YRYGEHYDSVRRINDNSEAPAH LQTDFQMLHQDESNKREKIKTK GMDSEDDLRDEVEDAVQKVCNA TGCSDFNLIVQNLEAENYNIES AIIAVLRMNQGKRNNAEENLEP SGRVLKQCGPLWEE GGSGARIFGNQGLNEGRTENNK AQASPSEENKANKNQLAKVTNK QRREQQWMEKKKRQEERHRHKA LESRGSHRDNNRSEAEANTQVT LVKTFAALNI	188	MSRKQAAKSRPGSGSRKAEA ERKRDERAARRALAKERRNR PESGGGGGCEEEFVSFANQL QALGLKLREVPGDGNCLFRA LGDQLEGHSRNHLKHRQETV DYMIKQREDFEPFVEDDIPF EKHVASLAKPGTFAGNDAIV AFARNHQLNVVIHQLNAPLW QIRGTEKSSVRELHIAYRYG EHYDSVRR
OTU7B_HUMAN OTU domain-containing protein 7B (Also referred to herein as Cezanne)	80	MTLDMDAVLSDFVRSTGAEPGL ARDLLEGKNWDVNAALSDFEQL RQVHAGNLPPSFSEGSGGSRTP EKGFSDREPTRPPRPILQRQDD IVQEKRLSRGISHASSSIVSLA RSHVSSNGGGGGSNEHPLEMPI CAFQLPDLTVYNEDFRSFIERD LIEQSMLVALEQAGRLNWWVSV DPTSQRLLPLATTGDGNCLLHA ASLGMWGFHDRDLMLRKALYAL MEKGVEKEALKRRWRWQQTQQN KESGLVYTEDEWQKEWNELIKL ASSEPRMHLGTNGANCGGVESS EEPVYESLEEFHVFVLAHVLRR PIVVVADTMLRDSGGEAFAPIP FGGIYLPLEVPASQCHRSPLVL AYDQAHFSALVSMEQKENTKEQ AVIPLTDSEYKLLPLHFAVDPG KGWEWGKDDSDNVRLASVILSL EVKLHLLHSYMNVKWIPLSSDA QAPLAQPESPTASAGDEPRSTP ESGDSDKESVGSSSTSNEGGRR KEKSKRDREKDKKRADSVANKL	189	MTLDMDAVLSDFVRSTGAEP GLARDLLEGKNWDVNAALSD FEQLRQVHAGNLPPSFSEGS GGSRTPEKGFSDREPTRPPR PILQRQDDIVQEKRLSRGIS HASSSIVSLARSHVSSNGGG GGSNEHPLEMPICAFQLPDL TVYNEDFRSFIERDLIEQSM LVALEQAGRLNWWVSVDPTS QRLLPLATTGDGNCLLHAAS LGMWGFHDRDLMLRKALYAL MEKGVEKEALKRRWRWQQTQ QNKESGLVYTEDEWQKEWNE LIKLASSEPRMHLGTNGANC GGVESSEEPVYESLEEFHVF VLAHVLRRPIVVVADTMLRD SGGEAFAPIPFGGIYLPLEV PASQCHRSPLVLAYDQAHFS AL
			293	PPSFSEGSGGSRTPEKGFSD REPTRPPRPILQRQDDIVQE KRLSRGISHASSSIVSLARS HVSSNGGGGGSNEHPLEMPI

		GSFGKTLGSKLKKNMGGLMHSK GSKPGGVGTGLGGSSGTETLEK KKKNSLKSWKGGKEEAAGDGPV SEKPPAESVGNGGSKYSQEVMQ SLSILRTAMQGEGKFIFVGTLK MGHRHQYQEEMIQRYLSDAEER FLAEQKQKEAERKIMNGGIGGG PPPAKKPEPDAREEQPTGPPAE SRAMAFSTGYPGDFTIPRPSGG GVHCQEPRRQLAGGPCVGGLPP YATFPRQCPPGRPYPHQDSIPS LEPGSHSKDGLHRGALLPPPYR VADSYSNGYREPPEPDGWAGGL RGLPPTQTKCKQPNCSFYGHPE TNNFCSCCYREELRRREREPDG ELLVHRF		CAFQLPDLTVYNEDFRSFIE RDLIEQSMLVALEQAGRLNW WVSVDPTSQRLLPLATTGDG NCLLHAASLGMWGFHDRDLM LRKALYALMEKGVEKEALKR RWRWQQTQQNKESGLVYTED EWQKEWNELIKLASSEPRMH LGTNGANCGGVESSEEPVYE SLEEFHVFVLAHVLRRPIVV VADTMLRDSGGEAFAPIPFG GIYLPLEVPASQCHRSPLVL AYDQAHFSALVSMEQKENTK EQAVIPLTDSEYKLLPLHFA VDPGKGWEWGKDDSDNVRLA SVILSLEVKLHLLHSYMNVK WIPLSSDAQAPLAQ
OTUD5_HUMAN OTU domain-containing protein 5	81	MTILPKKKPPPPDADPANEPPP PGPMPPAPRRGGGVGVGGGGTG VGGGDRDRDSGVVGARPRASPP PQGPLPGPPGALHRWALAVPPG AVAGPRPQQASPPPCGGPGGPG GGPGDALGAAAAGVGAAGVVVG VGGAVGVGGCCSGPGHSKRRRQ APGVGAVGGGSPEREEVGAGYN SEDEYEAAAARIEAMDPATVEQ QEHWFEKALRDKKGFIIKQMKE DGACLFRAVADQVYGDQDMHEV VRKHCMDYLMKNADYFSNYVTE DFTTYINRKRKNNCHGNHIEMQ AMAEMYNRPVEVYQ YSTGTSAVEPINTFHGIHQNED EPIRVSYHRNIHYNSVVNPNKA TIGVGLGLPSFKPGFAEQSLMK NAIKTSEESWIEQQMLEDKKRA TDWEATNEAIEEQVARESYLQW LRDQEKQARQVRGPSQPRKASA TCSSATAAASSGLEEWTSRSPR QRSSASSPEHPELHAELGMKPP SPGTVLALAKPPSPCAPGTSSQ FSAGADRATSPLVSLYPALECR ALIQQMSPSAFGLNDWDDDEIL ASVLAVSQQEYLDSMKKNKVHR DPPPDKS	190	MTILPKKKPPPPDADPANEP PPPGPMPPAPRRGGGVGVGG GGTGVGGGDRDRDSGVVGAR PRASPPPQGPLPGPPGALHR WALAVPPGAVAGPRPQQASP PPCGGPGGPGGGPGDALGAA AAGVGAAGVVVGVGGAVGVG GCCSGPGHSKRRRQAPGVGA VGGGSPEREEVGAGYNSEDE YEAAAARIEAMDPATVEQQE HWFEKALRDKKGFIIKQMKE DGACLFRAVADQVYGDQDMH EVVRKHCMDYLMKNADYFSN YVTEDFTTYINRKRKNNCHG NHIEMQAMAEMYNRPVEVYQ YSTGTSAVEPINTFHGIHQN EDEPIRVSYHRNIHYNSV
TNAP3_HUMAN Tumor necrosis factor alpha-induced protein 3	82	MAEQVLPQALYLSNMRKAVKIR ERTPEDIFKPTNGIIHHFKTMH RYTLEMFRTCQFCPQFREIIHK ALIDRNIQATLESQKKLNWCRE VRKLVALKTNGDGNCLMHATSQ YMWGVQDTDLVLRKALFSTLKE TDTRNFKFRWQLESLKSQEFVE TGLCYDTRNWNDEWDNLIKMAS	191	MAEQVLPQALYLSNMRKAVK IRERTPEDIFKPTNGIIHHF KTMHRYTLEMFRTCQFCPQF REIIHKALIDRNIQATLESQ KKLNWCREVRKLVALKTNGD GNCLMHATSQYMWGVQDTDL VLRKALFSTLKETDTRNFKF RWQLESLKSQEFVETGLCYD

		TDTPMARSGLQYNSLEEIHIFV LCNILRRPIIVISDKMLRSLES GSNFAPLKVGGIYLPLHWPAQE CYRYPIVLGYDSHHFVPLVTLK DSGPEIRAVPLVNRDRGRFEDL KVHFLTDPENEMKE KLLKEYLMVIEIPVQGWDHGTT HLINAAKLDEANLPKEINLVDD YFELVQHEYKKWQENSEQGRRE GHAQNPMEPSVPQLSLMDVKCE TPNCPFFMSVNTQPLCHECSER RQKNQNKLPKLNSKPGPEGLPG MALGASRGEAYEPLAWNPEEST GGPHSAPPTAPSPFLFSETTAM KCRSPGCPFTLNVQHNGFCERC HNARQLHASHAPDHTRHLDPGK CQACLQDVTRTFNGICSTCFKR TTAEASSSLSTSLPPSCHQRSK SDPSRLVRSPSPHSCHRAGNDA PAGCLSQAARTPGD RTGTSKCRKAGCVYFGTPENKG FCTLCFIEYRENKHFAAASGKV SPTASRFQNTIPCLGRECGTLG STMFEGYCQKCFIEAQNQRFHE AKRTEEQLRSSQRRDVPRTTQS TSRPKCARASCKNILACRSEEL CMECQHPNQRMGPGAHRGEPAP EDPPKQRCRAPACDHFGNAKCN GYCNECFQFKQMYG		TRNWNDEWDNLIKMASTDTP MARSGLQYNSLEEIHIFVLC NILRRPIIVISDKMLRSLES GSNFAPLKVGGIYLPLHWPA QECYRYPIVLGYDSHHFVPL
ZRAN1_HUMAN Ubiquitin thioesterase ZRANB1	83	MSERGIKWACEYCTYENWPSAI KCTMCRAQRPSGTIITEDPFKS GSSDVGRDWDPSSTEGGSSPLI CPDSSARPRVKSSYSMENANKW SCHMCTYLNWPRAIRCTQCLSQ RRTRSPTESPQSSGSGSRPVAF SVDPCEEYNDRNKLNTRTQHWT CSVCTYENWAKAKRCVVCDHPR PNNIEAIELAETEEASSIINEQ DRARWRGSCSSGNSQRRSPPAT KRDSEVKMDFQRIELAGAVGSK EELEVDFKKLKQIKNRMKKTDW LFLNACVGVVEGDLAAIEAYKS SGGDIARQLTADEV RLLNRPSAFDVGYTLVHLAIRF QRQDMLAILLTEVSQQAAKCIP AMVCPELTEQIRREIAASLHQR KGDFACYFLTDLVTFTLPADIE DLPPTVQEKLFDEVLDRDVQKE LEEESPIINWSLELATRLDSRL YALWNRTAGDCLLDSVLQATWG IYDKDSVLRKALHDSLHDCSHW	192	MSERGIKWACEYCTYENWPS AIKCTMCRAQRPSGTIITED PFKSGSSDVGRDWDPSSTEG GSSPLICPDSSARPRVKSSY SMENANKWSCHMCTYLNWPR AIRCTQCLSQRRTRSPTESP QSSGSGSRPVAFSVDPCEEY NDRNKLNTRTQHWTCSVCTY ENWAKAKRCVVCDHPRPNNI EAIELAETEEASSIINEQDR ARWRGSCSSGNSQRRSPPAT KRDSEVKMDFQRIELAGAVG SKEELEVDFKKLKQIKNRMK KTDWLFLNACVGVVEGDLAA IEAYKSSGGDIARQLTADEV RLLNRPSAFDVGYTLVHLAI RFQRQDMLAILLTEVSQQAA KCIPAMVCPELTEQIRREIA ASLHQRKGDFACYFLTDLVT FTLPADIEDLPPTVQEKLFD EVLDRDVQKELEEESPIINW SLELATRLDSRLYALWNRTA

		FYTRWKDWESWYSQSFGLHFSL REEQWQEDWAFILSLASQPGAS LEQTHIFVLAHILRRPIIVYGV KYYKSFRGETLGYTRFQGVYLP LLWEQSFCWKSPIALGYTRGHF SALVAMENDGYGNR GAGANLNTDDDVTITFLPLVDS ERKLLHVHFLSAQELGNEEQQE KLLREWLDCCVTEGGVLVAMQK SSRRRNHPLVTQMVEKWLDRYR QIRPCTSLSDGEEDEDDEDE		GDCLLDSVLQATWGIYDKDS VLRKALHDSLHDCSHWFYTR WKDWESWYSQSFGLHFSLRE EQWQEDWAFILSLASQPGAS LEQTHIFVLAHILRRPIIVY GVKYYKSFRGETLGYTRFQG VYLPLLWEQSFCWKSPIALG YTRGHFSAL
VCIP1_HUMAN Deubiquitinating protein VCIP135	84	MSQPPPPPPPLPPPPPPPEAPQ TPSSLASAAASGGLLKRRDRRI LSGSCPDPKCQARLFFPASGSV SIECTECGQRHEQQQLLGVEEV TDPDVVLHNLLRNALLGVTGAP KKNTELVKVMGLSNYHCKLLSP ILARYGMDKQTGRAKLLRDMNQ GELFDCALLGDRAFLIEPEHVN TVGYGKDRSGSLLYLHDTLEDI KRANKSQECLIPVHVDGDGHCL VHAVSRALVGRELFWHALRENL KQHFQQHLARYQALFHDFIDAA EWEDIINECDPLFVPPEGVPLG LRNIHIFGLANVLH RPIILLDSLSGMRSSGDYSATF LPGLIPAEKCTGKDGHLNKPIC IAWSSSGRNHYIPLVGIKGAAL PKLPMNLLPKAWGVPQDLIKKY IKLEEDGGCVIGGDRSLQDKYL LRLVAAMEEVFMDKHGIHPSLV ADVHQYFYRRTGVIGVQPEEVT AAAKKAVMDNRLHKCLLCGALS ELHVPPEWLAPGGKLYNLAKST HGQLRTDKNYSFPLNNLVCSYD SVKDVLVPDYGMSNLTACNWCH GTSVRKVRGDGSIVYLDGDRTN SRSTGGKCGCGFKHFWDGKEYD NLPEAFPITLEWGG RVVRETVYWFQYESDSSLNSNV YDVAMKLVTKHFPGEFGSEILV QKVVHTILHQTAKKNPDDYTPV NIDGAHAQRVGDVQGQESESQL PTKIILTGQKTKTLHKEELNMS KTERTIQQNITEQASVMQKRKT EKLKQEQKGQPRTVSPSTIRDG PSSAPATPTKAPYSPTTSKEKK IRITTNDGRQSMVTLKSSTTFF ELQESIAREFNIPPYLQCIRYG FPPKELMPPQAGMEKEPVPLQH GDRITIEILKSKAEGGQSAAAH	193	PASGSVSIECTECGQRHEQQ QLLGVEEVTDPDVVLHNLLR NALLGVTGAPKKNTELVKVM GLSNYHCKLLSPILARYGMD KQTGRAKLLRDMNQGELFDC ALLGDRAFLIEPEHVNTVGY GKDRSGSLLYLHDTLEDIKR ANKSQECLIPVHVDGDGHCL VHAVSRALVGRELFWHALRE NLKQHFQQHLARYQALFHDF IDAAEWEDIINECDPLFVPP EGVPLGLRNIHIFGLANVLH RPIILLDSLSGMRSSGDYSA TFLPGLIPAEKCTGKDGHLN KPICIAWSSSGRNHYIPL

		SAHTVKQEDIAVTGKLSSKELQ EQAEKEMYSLCLLA TLMGEDVWSYAKGLPHMFQQGG VFYSIMKKTMGMADGKHCTFPH LPGKTFVYNASEDRLELCVDAA GHFPIGPDVEDLVKEAVSQVRA EATTRSRESSPSHGLLKLGSGG VVKKKSEQLHNVTAFQGKGHSL GTASGNPHLDPRARETSVVRKH NTGTDFSNSSTKTEPSVFTASS SNSELIRIAPGVVTMRDGRQLD PDLVEAQRKKLQEMVSSIQASM DRHLRDQSTEQSPSDLPQRKTE VVSSSAKSGSLQTGLPESFPLT GGTENLNTETTDGCVADALGAA FATRSKAQRGNSVEELEEMDSQ DAEMTNTTEPMDHS		
UCHL3_HUMAN Ubiquitin carboxyl-terminal hydrolase isozyme L3	85	MEGQRWLPLEANPEVTNQFLKQ LGLHPNWQFVDVYGMDPELLSM VPRPVCAVLLLFPITEKYEVFR TEEEEKIKSQGQDVTSSVYFMK QTISNACGTIGLIHAIANNKDK MHFESGSTLKKFLEESVSMSPE ERARYLENYDAIRVTHETSAHE GQTEAPSIDEKVDLHFIALVHV DGHLYELDGRKPFPINHGETSD ETLLEDAIEVCKKFMERDPDEL RFNAIALSAA	194	QRWLPLEANPEVTNQFLKQL GLHPNWQFVDVYGMDPELLS MVPRPVCAVLLLFPITEKYE VFRTEEEEKIKSQGQDVTSS VYFMKQTISNACGTIGLIHA IANNKDKMHFESGSTLKKFL EESVSMSPEERARYLENYDA IRVTHETSAHEGQTEAPSID EKVDLHFIALVHVDGHLYEL DGRKPFPINHGETSDETLLE DAIEVCKKFMERDPDELRFN AIALSAA
UCHL1_HUMAN Ubiquitin carboxyl-terminal hydrolase isozyme L1	86	MQLKPMEINPEMLNKVLSRLGV AGQWRFVDVLGLEEESLGSVPA PACALLLLFPLTAQHENFRKKQ IEELKGQEVSPKVYFMKQTIGN SCGTIGLIHAVANNQDKLGFED GSVLKQFLSETEKMSPEDRAKC FEKNEAIQAAHDAVAQEGQCRV DDKVNFHFILFNNVDGHLYELD GRMPFPVNHGASSEDTLLKDAA KVCREFTEREQGEVRFSAVALC KAA	86	MQLKPMEINPEMLNKVLSRL GVAGQWRFVDVLGLEEESLG SVPAPACALLLLFPLTAQHE NFRKKQIEELKGQEVSPKVY FMKQTIGNSCGTIGLIHAVA NNQDKLGFEDGSVLKQFLSE TEKMSPEDRAKCFEKNEAIQ AAHDAVAQEGQCRVDDKVNF HFILFNNVDGHLYELDGRMP FPVNHGASSEDTLLKDAAKV CREFTEREQGEVRFSAVALC KAA
UCHL5_HUMAN Ubiquitin carboxyl-terminal hydrolase isozyme L5	87	MTGNAGEWCLMESDPGVFTELI KGFGCRGAQVEEIWSLEPENFE KLKPVHGLIFLFKWQPGEEPAG SVVQDSRLDTIFFAKQVINNAC ATQAIVSVLLNCTHQDVHLGET LSEFKEFSQSFDAAMKGLALSN SDVIRQVHNSFARQQMFEFDTK TSAKEEDAFHFVSYVPVNGRLY ELDGLREGPIDLGACNQDDWIS AVRPVIEKRIQKYSEGEIRFNL	195	GEWCLMESDPGVFTELIKGF GCRGAQVEEIWSLEPENFEK LKPVHGLIFLFKWQPGEEPA GSVVQDSRLDTIFFAKQVIN NACATQAIVSVLLNCTHQDV HLGETLSEFKEFSQSFDAAM KGLALSNSDVIRQVHNSFAR QQMFEFDTKTSAKEEDAFHF VSYVPVNGRLYELDGLREGP IDLGACNQDDWISAVRPVIE

		MAIVSDRKMIYEQKIAELQRQL AEEEPMDTDQGNSMLSAIQSEV AKNQMLIEEEVQKLKRYKIENI RRKHNYLPFIMELLKTLAEHQQ LIPLVEKAKEKQNAKKAQETK		KRIQKYSEGEIRFNLMAIVS DRK
ATX3_HUMAN Ataxin-3	88	MESIFHEKQEGSLCAQHCLNNL LQGEYFSPVELSSIAHQLDEEE RMRMAEGGVTSEDYRTFLQQPS GNMDDSGFFSIQVISNALKVWG LELILFNSPEYQRLRIDPINER SFICNYKEHWFTVRKLGKQWFN LNSLLTGPELISDTYLALFLAQ LQQEGYSIFVVKGDLPDCEADQ LLQMIRVQQMHRPKLIGEELAQ LKEQRVHKTDLERVLEANDGSG MLDEDEEDLQRALALSRQEIDM EDEEADLRRAIQLSMQGSSRNI SQDMTQTSGTNLTSEELRKRRE AYFEKQQQKQQQQQQQQQQGDL SGQSSHPCERPATSSGALGSDL GDAMSEEDMLQAAVTMSLETVR NDLKTEGKK	196	ESIFHEKQEGSLCAQHCLNN LLQGEYFSPVELSSIAHQLD EEERMRMAEGGVTSEDYRTF LQQPSGNMDDSGFFSIQVIS NALKVWGLELILFNSPEYQR LRIDPINERSFICNYKEHWF TVRKLGKQWFNLNSLLTGPE LISDTYLALFLAQLQQEGYS IFVVK
JOS2_HUMAN Josephin-2	89	MSQAPGAQPSPPTVYHERQRLE LCAVHALNNVLQQQLFSQEAAD EICKRLAPDSRLNPHRSLLGTG NYDVNVIMAALQGLGLAAVWWD RRRPLSQLALPQVLGLILNLPS PVSLGLLSLPLRRRHWVALRQV DGVYYNLDSKLRAPEALGDEDG VRAFLAAALAQGLCEVLLVVTK EVEEKGSWLRTD	197	PTVYHERQRLELCAVHALNN VLQQQLFSQEAADEICKRLA PDSRLNPHRSLLGTGNYDVN VIMAALQGLGLAAVWWDRRR PLSQLALPQVLGLILNLPSP VSLGLLSLPLRRRHWVALRQ VDGVYYNLDSKLRAPEALGD EDGVRAFLAAALAQGLCEVL LVV
JOS1_HUMAN Josephin-1	90	MSCVPWKGDKAKSESLELPQAA PPQIYHEKQRRELCALHALNNV FQDSNAFTRDTLQEIFQRLSPN TMVTPHKKSMLGNGNYDVNVIM AALQTKGYEAVWWDKRRDVGVI ALTNVMGFIMNLPSSLCWGPLK LPLKRQHWICVREVGGAYYNLD SKLKMPEWIGGESELRKFLKHH LRGKNCELLLVVPEEVEAHQSW RTDV	198	PQAAPPQIYHEKQRRELCAL HALNNVFQDSNAFTRDTLQE IFQRLSPNTMVTPHKKSMLG NGNYDVNVIMAALQTKGYEA VWWDKRRDVGVIALTNVMGF IMNLPSSLCWGPLKLPLKRQ HWICVREVGGAYYNLDSKLK MPEWIGGESELRKFLKHHLR GKNCELLLVV
ATX3L_HUMAN Ataxin-3-like protein	91	MDFIFHEKQEGFLCAQHCLNNL LQGEYFSPVELASIAHQLDEEE RMRMAEGGVTSEEYLAFLQQPS ENMDDTGFFSIQVISNALKFWG LEIIHFNNPEYQKLGIDPINER SFICNYKQHWFTIRKFGKHWFN LNSLLAGPELISDTCLANFLAR LQQQAYSVFVVKGDLPDCEADQ LLQIISVEEMDTPKLNGKKLVK QKEHRVYKTVLEKVSEESDESG	199	DFIFHEKQEGFLCAQHCLNN LLQGEYFSPVELASIAHQLD EEERMRMAEGGVTSEEYLAF LQQPSENMDDTGFFSIQVIS NALKFWGLEIIHFNNPEYQK LGIDPINERSFICNYKQHWF TIRKFGKHWFNLNSLLAGPE LISDTCLANFLARLQQQAYS VFVVK

		TSDQDEEDFQRALELSRQETNR EDEHLRSTIELSMQGSSGNTSQ DLPKTSCVTPASEQPKKIKEDY FEKHQQEQKQQQQQSDLPGHSS YLHERPTTSSRAIESDLSDDIS EGTVQAAVDTILEIMRKNLKIK GEK		
MINY3_HUMAN Ubiquitin carboxyl-terminal hydrolase MINDY-3	92	MSELTKELMELVWGTKSSPGLS DTIFCRWTQGFVFSESEGSALE QFEGGPCAVIAPVQAFLLKKLL FSSEKSSWRDCSEEEQKELLCH TLCDILESACCDHSGSYCLVSW LRGKTTEETASISGSPAESSCQ VEHSSALAVEELGFERFHALIQ KRSFRSLPELKDAVLDQYSMWG NKFGVLLFLYSVLLTKGIENIK NEIEDASEPLIDPVYGHGSQSL INLLLTGHAVSNVWDGDRECSG MKLLGIHEQAAVGFLTLMEALR YCKVGSYLKSPKFPIWIVGSET HLTVFFAKDMALVA PEAPSEQARRVFQTYDPEDNGF IPDSLLEDVMKALDLVSDPEYI NLMKNKLDPEGLGIILLGPFLQ EFFPDQGSSGPESFTVYHYNGL KQSNYNEKVMYVEGTAVVMGFE DPMLQTDDTPIKRCLQTKWPYI ELLWTTDRSPSLN	200	CRWTQGFVFSESEGSALEQF EGGPCAVIAPVQAFLLKKLL FSSEKSSWRDCSEEEQKELL CHTLCDILESACCDHSGSYC LVSWLRGKTTEETASISGSP AESSCQVEHSSALAVEELGF ERFHALIQKRSFRSLPELKD AVLDQYSMWGNKFG VLLFLYSVLLTKGIENIKNE IEDASEPLIDPVYGHGSQSL INLLLTGHAVSNVWDGDREC SGMKLLGIHEQAAVGFLTLM EALRYCKVGSYLKSPKFPIW IVGSETHLTVFFAKDMALVA PEAPSEQARRVFQTYDPEDN GFIPDSLLEDVMKALDLVSD PEYINLMKNKLDPEGLGIIL LGPFLQEFFPDQGSSGPESF TVYHYNGLKQSNYNEKVMYV EGTAVVMGFEDPMLQTDDTP IKRCLQTKWPYIELLWTTDR SPSLN
MINY1_HUMAN Ubiquitin carboxyl-terminal hydrolase MINDY-1	93	MEYHQPEDPAPGKAGTAEAVIP ENHEVLAGPDEHPQDTDARDAD GEARErEPADQALLPSQCGDNL ESPLPEASSAPPGPTLGTLPEV ETIRACSMPQELPQSPRTRQPE PDFYCVKWIPWKGEQTPIITQS TNGPCPLLAIMNILFLQWKVKL PPQKEVITSDELMAHLGNCLLS IKPQEKSEGLQLNFQQNVDDAM TVLPKLATGLDVNVRFTGVSDF EYTPECSVFDLLGIPLYHGWLV DPQSPEAVRAVGKLSYNQLVER IITCKHSSDTNLVTEGLIAEQF LETTAAQLTYHGLC ELTAAAKEGELSVFFRNNHFST MTKHKSHLYLLVTDQGFLQEEQ VVWESLHNVDGDSCFCDSDFHL SHSLGKGPGAEGGSGSPETQLQ VDQDYLIALSLQQQQPRGPLGL TDLELAQQLQQEEYQQQQAAQP VRMRTRVLSLQGRGATSGRPAG ERRQRPKHESDCILL	201	YCVKWIPWKGEQTPIITQST NGPCPLLAIMNILFLQWKVK LPPQKEVITSDELMAHLGNC LLSIKPQEKSEGLQLNFQQN VDDAMTVLPKLATGLDVNVR FTGVSDFEYTPECSVFDLLG IPLYHGWLVDPQSPEAVRAV GKLSYNQLVERIITCKHSSD TNLVTEGLIAEQFLETTAAQ LTYHGLCELTAAAKEGELSV FFRNNHFSTMTKHKSHLYLL VTDQGFLQEEQVVWESLHNV DGDSCFCDSDFHLSHSLGKG PGAEGGSGSPETQLQVDQDY LIALSLQQQQPRGPLGLTDL ELAQQLQQEEYQQQQAAQPV RMRTRVLSLQGRGATSGRPA GERRQRPKHESDCILL

MINY2_HUMAN Ubiquitin carboxyl-terminal hydrolase MINDY-2	94	MESSPESLQPLEHGVAAGPASG TGSSQEGLQETRLAAGDGPGVW AAETSGGNGLGAAAARRSLPDS ASPAGSPEVPGPCSSSAGLDLK DSGLESPAAAEAPLRGQYKVTA SPETAVAGVGHELGTAGDAGAR PDLAGTCQAELTAAGSEEPSSA GGLSSSCSDPSPPGESPSLDSL ESFSNLHSFPSSCEFNSEEGAE NRVPEEEEGAAVLPGAVPLCKE EEGEETAQVLAASKERFPGQSV YHIKWIQWKEENTPIITQNENG PCPLLAILNVLLLAWKVKLPPM MEIITAEQLMEYLG DYMLDAKPKEISEIQRLNYEQN MSDAMAILHKLQTGLDVNVRFT GVRVFEYTPECIVFDLLDIPLY HGWLVDPQIDDIVKAVGNCSYN QLVEKIISCKQSDNSELVSEGF VAEQFLNNTATQLTYHGLCELT STVQEGELCVFFRNNHFSTMTK YKGQLYLLVTDQGFLTEEKVVW ESLHNVDGDGNFCDSEFHLRPP SDPETVYKGQQDQIDQDYLMAL SLQQEQQSQEINWEQIPEGISD LELAKKLQEEEDRRASQYYQEQ EQAAAAAAAASTQAQQGQPAQA SPSSGRQSGNSERKRKEPREKD KEKEKEKNSCVIL	202	YHIKWIQWKEENTPIITQNE NGPCPLLAILNVLLLAWKVK LPPMMEIITAEQLMEYLGDY MLDAKPKEISEIQRLNYEQN MSDAMAILHKLQTGLDVNVR FTGVRVFEYTPECIVFDLLD IPLYHGWLVDPQIDDIVKAV GNCSYNQLVEKIISCKQSDN SELVSEGFVAEQFLNNTATQ LTYHGLCELTSTVQEGELCV FFRNNHFSTMTKYKGQLYLL VTDQGFLTEEKVVWESLHNV DGDGNFCDSEFHLRPPSDPE TVYKGQQDQIDQDYLMALSL QQEQQSQEINWEQIPEGISD LELAKKLQEEEDRRASQYYQ EQEQAAAAAAAASTQAQQGQ PAQASPSSGRQSGNSERKRK EPREKDKEKEKEKNSCVIL
MINY4_HUMAN Probable ubiquitin carboxyl-terminal hydrolase MINDY-4	95	MDSLFVEEVAASLVREFLSRKG LKKTCVTMDQERPRSDLSINNR NDLRKVLHLEFLYKENKAKENP LKTSLELITRYFLDHFGNTANN FTQDTPIPALSVPKKNNKVPSR CSETTLVNIYDLSDEDAGWRTS LSETSKARHDNLDGDVLGNFVS SKRPPHKSKPMQTVPGETPVLT SAWEKIDKLHSEPSLDVKRMGE NSRPKSGLIVRGMMSGPIASSP QDSFHRHYLRRSSPSSSSTQPQ EESRKVPELFVCTQQDILASSN SSPSRTSLGQLSELTVERQKTT ASSPPHLPSKRLPP WDRARPRDPSEDTPAVDGSTDT DRMPLKLYLPGGNSRMTQERLE RAFKRQGSQPAPVRKNQLLPSD KVDGELGALRLEDVEDELIREE VILSPVPSVLKLQTASKPIDLS VAKEIKTLLFGSSFCCFNEEWK LQSFSFSNTASLKYGIVQNKGG PCGVLAAVQGCVLQKLLFEGDS	203	FCCFNEEWKLQSFSFSNTAS LKYGIVQNKGGPCGVLAAVQ GCVLQKLLFEGDSKADCAQG LQPSDAHRTRCLVLALADIV WRAGGRERAVVALASRTQQF SPTGKYKADGVLETLTLHSL TCYEDLVTFLQQSIHQFEVG PYGCILLTLSAILSRSTELI RQDFDVPTSHLIGAHGYCTQ ELVNLLLTGKAVSNVFNDVV ELDSGDGNITLLRGIAARSD IGFLSLFEHYNMCQVGCFLK TPRFPIWVVCSESHFSILFS LQPGLLRDWRTERLFDLYYY DGLANQQEQIRLTIDTTQTI SEDTDNDLVPPLELCIRTKW KGASVNWNGSDPIL

		KADCAQGLQPSDAHRTRCLVLA LADIVWRAGGRERAVVALASRT QQFSPTGKYKADGVLETLTLHS LTCYEDLVTFLQQSIHQFEVGP YGCILLTLSAILSRSTELIRQD FDVPTSHLIGAHGY CTQELVNLLLTGKAVSNVFNDV VELDSGDGNITLLRGIAARSDI GFLSLFEHYNMCQVGCFLKTPR FPIWVVCSESHFSILFSLQPGL LRDWRTERLFDLYYYDGLANQQ EQIRLTIDTTQTISEDTDNDLV PPLELCIRTKWKGASVNWNGSD PIL		
STABP_HUMAN STAM-binding protein	96	MSDHGDVSLPPEDRVRALSQLG SAVEVNEDIPPRRYFRSGVEII RMASIYSEEGNIEHAFILYNKY ITLFIEKLPKHRDYKSAVIPEK KDTVKKLKEIAFPKAEELKAEL LKRYTKEYTEYNEEKKKEAEEL ARNMAIQQELEKEKQRVAQQKQ QQLEQEQFHAFEEMIRNQELEK ERLKIVQEFGKVDPGLGGPLVP DLEKPSLDVFPTLTVSSIQPSD CHTTVRPAKPPVVDRSLKPGAL SNSESIPTIDGLRHVVVPGRLC PQFLQLASANTARGVETCGILC GKLMRNEFTITHVL IPKQSAGSDYCNTENEEELFLI QDQQGLITLGWIHTHPTQTAFL SSVDLHTHCSYQMMLPESVAIV CSPKFQETGFFKLTDHGLEEIS SCRQKGFHPHSKDPPLFCSCSH VTVVDRAVTITDLR	204	VVPGRLCPQFLQLASANTAR GVETCGILCGKLMRNEFTIT HVLIPKQSAGSDYCNTENEE ELFLIQDQQGLITLGWIHTH PTQTAFLSSVDLHTHCSYQM MLPESVAIVCSPKFQETGFF KLTDHGLEEISSCRQKGFHP HSKDPPLFCSCSHVTVVDRA VTITDLR
MPND_HUMAN MPN domain-containing protein	97	MAAPEPLSPAGGAGEEAPEEDE DEAEAEDPERPNAGAGGGRSGG GGSSVSGGGGGGGAGAGGCGGP GGALTRRAVTLRVLLKDALLEP GAGVLSIYYLGKKFLGDLQPDG RIMWQETGQTFNSPSAWATHCK KLVNPAKKSGCGWASVKYKGQK LDKYKATWLRLHQLHTPATAAD ESPASEGEEEELLMEEEEEDVL AGVSAEDKSRRPLGKSPSEPAH PEATTPGKRVDSKIRVPVRYCM LGSRDLARNPHTLVEVTSFAAI NKFQPFNVAVSSNVLFLLDFHS HLTRSEVVGYLGGR WDVNSQMLTVLRAFPCRSRLGD AETAAAIEEEIYQSLFLRGLSL VGWYHSHPHSPALPSLQDIDAQ	205	VAVSSNVLFLLDFHSHLTRS EVVGYLGGRWDVNSQMLTVL RAFPCRSRLGDAETAAAIEE EIYQSLFLRGLSLVGWYHSH PHSPALPSLQDIDAQMDYQL RLQGSSNGFQPCLALLCSPY YSGNPGPESKISPFWVMPPP EMLLVEFYKGSPDLVRLQEP WSQEHTYLDKLKISLASRTP KDQSLCHVLEQVCGVLKQGS

		MDYQLRLQGSSNGFQPCLALLC SPYYSGNPGPESKISPFWVMPP PEMLLVEFYKGSPDLVRLQEPW SQEHTYLDKLKISLASRTPKDQ SLCHVLEQVCGVLKQGS		
EMC9_HUMAN ER membrane protein complex subunit 9	98	MGEVEISALAYVKMCLHAARYP HAAVNGLFLAPAPRSGECLCLT DCVPLFHSHLALSVMLEVALNQ VDVWGAQAGLVVAGYYHANAAV NDQSPGPLALKIAGRIAEFFPD AVLIMLDNQKLVPQPRVPPVIV LENQGLRWVPKDKNLVMWRDWE ESRQMVGALLEDRAHQHLVDFD CHLDDIRQDWTNQRLNTQITQW VGPTNGNGNA	206	ALAYVKMCLHAARYPHAAVN GLFLAPAPRSGECLCLTDCV PLFHSHLALSVMLEVALNQV DVWGAQAGLVVAGYYHANAA VNDQSPGPLALKIAGRIAEF FPDAVLIMLDNQKLVPQPRV PPVIVLENQGLRWVPKDKNL VMWRDWEESRQMVGALLEDR AHQHLVDFDCHLDDIRQDWT NQRLNTQITQWVGPTNGNGN A
PSDE_HUMAN 26S proteasome non-ATPase regulatory subunit 14	99	MDRLLRLGGGMPGLGQGPPTDA PAVDTAEQVYISSLALLKMLKH GRAGVPMEVMGLMLGEFVDDYT VRVIDVFAMPQSGTGVSVEAVD PVFQAKMLDMLKQTGRPEMVVG WYHSHPGFGCWLSGVDINTQQS FEALSERAVAVVVDPIQSVKGK VVIDAFRLINANMMVLGHEPRQ TTSNLGHLNKPSIQALIHGLNR HYYSITINYRKNELEQKMLLNL HKKSWMEGLTLQDYSEHCKHNE SVVKEMLELAKNYNKAVEEEDK MTPEQLAIKNVGKQDPKRHLEE HVDVLMTSNIVQCLAAMLDTVV FK	207	QVYISSLALLKMLKHGRAGV PMEVMGLMLGEFVDDYTVRV IDVFAMPQSGTGVSVEAVDP VFQAKMLDMLKQTGRPEMVV GWYHSHPGFGCWLSGVDINT QQSFEALSERAVAVVVDPIQ SVKGKVVIDAFRLINANMMV LGHEPRQTTSNLGHLNKPSI QALIHGLNRHYYSITINYRK NELEQKMLLNLHKKSWMEGL TLQDYSEHCKHNESVVKEML ELAKNYNKAVEEEDKMTPEQ LAIKNVGKQDPKRHLEEHVD VLMTSNIVQCLAAMLDTVVF K
MYSM1_HUMAN Histone H2A deubiquitinase MYSM1	100	MAAEEADVDIEGDVVAAAGAQP GSGENTASVLQKDHYLDSSWRT ENGLIPWTLDNTISEENRAVIE KMLLEEEYYLSKKSQPEKVWLD QKEDDKKYMKSLQKTAKIMVHS PTKPASYSVKWTIEEKELFEQG LAKFGRRWTKISKLIGSRTVLQ VKSYARQYFKNKVKCGLDKETP NQKTGHNLQVKNEDKGTKAWTP SCLRGRADPNLNAVKIEKLSDD EEVDITDEVDELSSQTPQKNSS SDLLLDFPNSKMHETNQGEFIT SDSQEALFSKSSRGCLQNEKQD ETLSSSEITLWTEK QSNGDKKSIELNDQKFNELIKN CNKHDGRGIIVDARQLPSPEPC EIQKNLNDNEMLFHSCQMVEES HEEEELKPPEQEIEIDRNIIQE EEKQAIPEFFEGRQAKTPERYL KIRNYILDQWEICKPKYLNKTS	208	QVKVASEALLIMDLHAHVSM AEVIGLLGGRYSEVDKVVEV CAAEPCNSLSTGLQCEMDPV SQTQASETLAVRGFSVIGWY HSHPAFDPNPSLRDIDTQAK YQSYFSRGGAKFIGMIVSPY NRNNPLPYSQITCLVISEEI SPDGSYRLPYKFEVQQMLEE PQWGLVFEKTRWIIEKYRLS HSSVPMDKIFRRDSDLTCLQ KLLECMRKTLSKVTNCFMAE EFLTEIENLFLSNYKSNQEN GVTEENCTKELLM

		VRPGLKNCGDVNCIGRIHTYLE LIGAINFGCEQAVYNRPQTVDK VRIRDRKDAVEAYQLAQRLQSM RTRRRRVRDPWGNWCDAKDLEG QTFEHLSAEELAKRREEEKGRP VKSLKVPRPTKSSFDPFQLIPC NFFSEEKQEPFQVKVASEALLI MDLHAHVSMAEVIG LLGGRYSEVDKVVEVCAAEPCN SLSTGLQCEMDPVSQTQASETL AVRGFSVIGWYHSHPAFDPNPS LRDIDTQAKYQSYFSRGGAKFI GMIVSPYNRNNPLPYSQITCLV ISEEISPDGSYRLPYKFEVQQM LEEPQWGLVFEKTRWIIEKYRL SHSSVPMDKIFRRDSDLTCLQK LLECMRKTLSKVTNCFMAEEFL TEIENLFLSNYKSNQENGVTEE NCTKELLM		
ABRX2_HUMAN BRISC complex subunit Abraxas 2	101	MAASISGYTFSAVCFHSANSNA DHEGFLLGEVRQEETFSISDSQ ISNTEFLQVIEIHNHQPCSKLF SFYDYASKVNEESLDRILKDRR KKVIGWYRFRRNTQQQMSYREQ VLHKQLTRILGVPDLVFLLFSF ISTANNSTHALEYVLFRPNRRY NQRISLAIPNLGNTSQQEYKVS SVPNTSQSYAKVIKEHGTDFFD KDGVMKDIRAIYQVYNALQEKV QAVCADVEKSERVVESCQAEVN KLRRQITQRKNEKEQERRLQQA VLSRQMPSESLDPAFSPRMPSS GFAAEGRSTLGDAE ASDPPPPYSDFHPNNQESTLSH SRMERSVFMPRPQAVGSSNYAS TSAGLKYPGSGADLPPPQRAAG DSGEDSDDSDYENLIDPTEPSN SEYSHSKDSRPMAHPDEDPRNT QTSQI	209	AVCFHSANSNADHEGFLLGE VRQEETFSISDSQISNTEFL QVIEIHNHQPCSKLFSFYDY ASKVNEESLDRILKDRRKKV IGWYRFRRNTQQQMSYREQV LHKQLTRIL GVPDLVFLLFSFISTANNST HALEYVLFRPNRRYNQRISL AIPNLGNTSQQEYKVSSVPN TSQSYAKVIKEHGTDFFDKD GVMKDIRAIYQVYNALQEKV QAVCADVEKSERVVESCQAE VNKLRRQITQRKNEKEQERR LQQAVLSRQMPSESLDPAFS PRMPSSGFAAEGRSTLGDAE ASDPPPPYSDFHPNNQESTL SHSRMERSVFMPRPQAVGSS NYASTSAGLKYPGSGADLPP PQRAAGDSGEDSDDSDYENL IDPTEPSNSEYSHSKDSRPM AHPDEDPRNTQTSQI
PRP8_HUMAN Pre-mRNA-processing-splicing factor 8	102	MAGVFPYRGPGNPVPGPLAPLP DYMSEEKLQEKARKWQQLQAKR YAEKRKFGFVDAQKEDMPPEHV RKIIRDHGDMTNRKFRHDKRVY LGALKYMPHAVLKLLENMPMPW EQIRDVPVLYHITGAISFVNEI PWVIEPVYISQWGSMWIMMRRE KRDRRHFKRMRFPPFDDEEPPL DYADNILDVEPLEAIQLELDPE EDAPVLDWFYDHQPLRDSRKYV NGSTYQRWQFTLPMMSTLYRLA	210	FNPRTGQLFLKIIHTSVWAG QKRLGQLAKWKTAEEVAALI RSLPVEEQPKQIIVTRKGML DPLEVHLLDFPNIVIKGSEL QLPFQACLKVEKFGDLILKA TEPQMVLFNLYDDWLKTISS YTAFSRLILILRALHVNNDR AKVILKPDKTTITEPHHIWP TLTDEEWIKVEVQLKDLILA DYGKKNNVNVASLTQSEIRD IILGMEISAPSQQRQQIAEI

		NQLLTDLVDDNYFYLFDLKAFF TSKALNMAIPGGPKFEPLVRDI NLQDEDWNEFNDIN KIIIRQPIRTEYKIAFPYLYNN LPHHVHLTWYHTPNVVFIKTED PDLPAFYFDPLINPISHRHSVK SQEPLPDDDEEFELPEFVEPFL KDTPLYTDNTANGIALLWAPRP FNLRSGRTRRALDIPLVKNWYR EHCPAGQPVKVRVSYQKLLKYY VLNALKHRPPKAQKKRYLFRSF KATKFFQSTKLDWVEVGLQVCR QGYNMLNLLIHRKNLNYLHLDY NFNLKPVKTLTTKERKKSRFGN AFHLCREVLRLTKLVVDSHVQY RLGNVDAFQLADGLQYIFAHVG QLTGMYRYKYKLMR QIRMCKDLKHLIYYRFNTGPVG KGPGCGFWAAGWRVWLFFMRGI TPLLERWLGNLLARQFEGRHSK GVAKTVTKQRVESHFDLELRAA VMHDILDMMPEGIKQNKARTIL QHLSEAWRCWKANIPWKVPGLP TPIENMILRYVKAKADWWTNTA HYNRERIRRGATVDKTVCKKNL GRLTRLYLKAEQERQHNYLKDG PYITAEEAVAVYTTTVHWLESR RFSPIPFPPLSYKHDTKLLILA LERLKEAYSVKSRLNQSQREEL GLIEQAYDNPHEALSRIKRHLL TQRAFKEVGIEFMD LYSHLVPVYDVEPLEKITDAYL DQYLWYEADKRRLFPPWIKPAD TEPPPLLVYKWCQGINNLQDVW ETSEGECNVMLESRFEKMYEKI DLTLLNRLLRLIVDHNIADYMT AKNNVVINYKDMNHTNSYGIIR GLQFASFIVQYYGLVMDLLVLG LHRASEMAGPPQMPNDFLSFQD IATEAAHPIRLFCRYIDRIHIF FRFTADEARDLIQRYLTEHPDP NNENIVGYNNKKCWPRDARMRL MKHDVNLGRAVFWDIKNRLPRS VTTVQWENSFVSVYSKDNPNLL FNMCGFECRILPKC RTSYEEFTHKDGVWNLQNEVTK ERTAQCFLRVDDESMQRFHNRV RQILMASGSTTFTKIVNKWNTA LIGLMTYFREAVVNTQELLDLL VKCENKIQTRIKIGLNSKMPSR FPPVVFYTPKELGGLGMLSMGH		EKQTKEQSQLTATQTRTVNK HGDEIITSTTSNYETQTFSS KTEWRVRAISAANLHLRTNH IYVSSDDIKETGYTYILPKN VLKKFICISDLRAQIAGYLY GVSPPDNPQVKEIRCIVMVP QWGTHQTVHLPGQLPQHEYL KEMEPLGWIHTQPNESPQLS PQDVTTHAKIMADNPSWDGE KTIIITCSFTPGSCTLTAYK LTPSGYEWGRQNTDKGNNPK GYLPSHYERVQMLLSDRFLG FFMVPAQSSWNYNFMGVRHD PNMKYELQLANPKEFYHEVH RPSHFLNFALLQEGEVYSAD REDLYA

		VLIPQSDLRWSKQTDVGITHFR SGMSHEEDQLIPNLYRYIQPWE SEFIDSQRVWAEYALKRQEAIA QNRRLTLEDLEDSWDRGIPRIN TLFQKDRHTLAYDKGWRVRTDF KQYQVLKQNPFWWTHQRHDGKL WNLNNYRTDMIQALGGVEGILE HTLFKGTYFPTWEG LFWEKASGFEESMKWKKLTNAQ RSGLNQIPNRRFTLWWSPTINR ANVYVGFQVQLDLTGIFMHGKI PTLKISLIQIFRAHLWQKIHES IVMDLCQVFDQELDALEIETVQ KETIHPRKSYKMNSSCADILLF ASYKWNVSRPSLLADSKDVMDS TTTQKYWIDIQLRWGDYDSHDI ERYARAKFLDYTTDNMSIYPSP TGVLIAIDLAYNLHSAYGNWFP GSKPLIQQAMAKIMKANPALYV LRERIRKGLQLYSSEPTEPYLS SQNYGELFSNQIIWFVDDTNVY RVTIHKTFEGNLTT KPINGAIFIFNPRTGQLFLKII HTSVWAGQKRLGQLAKWKTAEE VAALIRSLPVEEQPKQIIVTRK GMLDPLEVHLLDFPNIVIKGSE LQLPFQACLKVEKFGDLILKAT EPQMVLFNLYDDWLKTISSYTA FSRLILILRALHVNNDRAKVIL KPDKTTITEPHHIWPTLTDEEW IKVEVQLKDLILADYGKKNNVN VASLTQSEIRDIILGMEISAPS QQRQQIAEIEKQTKEQSQLTAT QTRTVNKHGDEIITSTTSNYET QTFSSKTEWRVRAISAANLHLR TNHIYVSSDDIKET GYTYILPKNVLKKFICISDLRA QIAGYLYGVSPPDNPQVKEIRC IVMVPQWGTHQTVHLPGQLPQH EYLKEMEPLGWIHTQPNESPQL SPQDVTTHAKIMADNPSWDGEK TIIITCSFTPGSCTLTAYKLTP SGYEWGRQNTDKGNNPKGYLPS HYERVQMLLSDRFLGFFMVPAQ SSWNYNFMGVRHDPNMKYELQL ANPKEFYHEVHRPSHFLNFALL QEGEVYSADREDLYA		
NPL4_HUMAN Membrane protein localization	103	MAESIIIRVQSPDGVKRITATK RETAATFLKKVAKEFGFQNNGF SVYINRNKTGEITASSNKSLNL LKIKHGDLLFLFPSSLAGPSSE	211	QPSAITLNRQKYRHVDNIMF ENHTVADRFLDFWRKTGNQH FGYLYGRYTEHKDIPLGIRA EVAAIYEPPQIGTQNSLELL

protein 4 homolog		METSVPPGFKVFGAPNVVEDEI DQYLSKQDGKIYRSRDPQLCRH GPLGKCVHCVPLEPFDEDYLNH LEPPVKHMSFHAYIRKLTGGAD KGKFVALENISCKIKSGCEGHL PWPNGICTKCQPSAITLNRQKY RHVDNIMFENHTVADRFLDFWR KTGNQHFGYLYGRYTEHKDIPL GIRAEVAAIYEPPQIGTQNSLE LLEDPKAEVVDEIA		EDPKAEVVDEIAAKLGLRKV GWIFTDLVSEDTRKGTVRYS RNKDTYFLSSEECITAGDFQ NKHPNMCRLSPDGHFGSKFV TAVATGGPDNQVHFEGYQVS NQCMALVRDECLLPCKDAPE LGYAKESSSEQYVPDVFYKD VDKFGNEITQLARPLPVEYL IIDITTTFPKDPVYTFSISQ NPFPIENRDVLGETQDFHSL ATYLSQNTSSVFLDTISDFH LLLFLVTNEVMPLQDSISLL LEAVRTRNEELAQTWKRSEQ WATIEQLCSTVGGQLPGLHE YGAVGGSTHTATAAMWACQH CTFMNQPGTGHCEMCSLPRT
EMC8_HUMAN ER membrane protein complex subunit 8	104	AKLGLRKVGWIFTDLVSEDTRK GTVRYSRNKDTYFLSSEECITA GDFQNKHPNMCRLSPDGHFGSK FVTAVATGGPDNQVHFEGYQVS NQCMALVRDECLLPCKDAPELG YAKESSSEQYVPDVFYKDVDKF GNEITQLARPLPVEYLIIDITT TFPKDPVYTFSISQNPFPIENR DVLGETQDFHSLATYLSQNTSS VFLDTISDFHLLLFLVTNEVMP LQDSISLLLEAVRTRNEELAQT WKRSEQWATIEQLCSTVGGQLP GLHEYGAVGGSTHTATAAMWAC QHCTFMNQPGTGHCEMCSLPRT	212	TQAYCKMVLHGAKYPHCAVN GLLVAEKQKPRKEHLPLGGP GAHHTLFVDCIPLFHGTLAL APMLEVALTLIDSWCKDHSY VIAGYYQANERVKDASPNQV AEKVASRIAEGFSDTALIMV DNTKFTMDCVAPTIHVYEHH ENRWRCRDPHHDYCEDWPEA QRISASLLDSRSYETLVDFD NHLDDIRNDWTNPEINKAVL HLC
ABRX1_HUMAN BRCA1-A complex subunit Abraxas 1	105	MPGVKLTTQAYCKMVLHGAKYP HCAVNGLLVAEKQKPRKEHLPL GGPGAHHTLFVDCIPLFHGTLA LAPMLEVALTLIDSWCKDHSYV IAGYYQANERVKDASPNQVAEK VASRIAEGFSDTALIMVDNTKF TMDCVAPTIHVYEHHENRWRCR DPHHDYCEDWPEAQRISASLLD SRSYETLVDFDNHLDDIRNDWT NPEINKAVLHLC	213	MEGESTSAVLSGFVLGALAFQH LNTDSDTEGFLLGEVKGEAKNS ITDSQMDDVEVVYTIDIQKYIP CYQLFSFYNSSGEVNEQALKKI LSNVKKNVVGWYKFRRHSDQIM TFRERLLHKNLQEHFSNQDLVF LLLTPSIITESCSTHRLEHSLY KPQKGLFHRVPLVVANLGMSEQ LGYKTVSGSCMSTGFSRAVQTH SSKFFEEDGSLKEVHKINEMYA SLQEELKSICKKVEDSEQAVDK LVKDVNRLKREIEKRRGAQIQA AREKNIQKDPQENIFLCQALRT FFPNSEFLHSCVMS LKNRHVSKSSCNYNHHLDVVDN LTLMVEHTDIPEASPASTPQII	GFVLGALAFQHLNTDSDTEG FLLGEVKGEAKNSITDSQMD DVEVVYTIDIQKYIPCYQLF SFYNSSGEVNEQALKKILSN VKKNVVGWYKFRRHSDQIMT FRERLLHKNLQEHFSNQDLV FLLLTPSIITESCSTHRLEH SLYKPQKGLFHRVPLVVANL GMSEQLGYKTVSGSCMSTGF SRAVQTHSSKFFEEDGSLKE VHKINEMYASLQEELKSICK KVEDSEQAVDKLVKDVNRLK REIEKRRGAQIQAAREKNIQ KDPQENIFLCQALRTFFPNS EFLHSCVMSLKNRHVSKSSC NYNHHLDVVDNLTLMVEHTD

		KHKALDLDDRWQFKRSRLLDTQ DKRSKADTGSSNQDKASKMSSP ETDEEIEKMKGFGEYSRSPTF		IPEASPASTPQIIKHKALDL DDRWQFKRSRLLDTQDKRSK ADTGSSNQDKASKMSSPETD EEIEKMKGFGEYSRSPTF
STALP_HUMAN AMSH-like protease	106	MDQPFTVNSLKKLAAMPDHTDV SLSPEERVRALSKLGCNITISE DITPRRYFRSGVEMERMASVYL EEGNLENAFVLYNKFITLFVEK LPNHRDYQQCAVPEKQDIMKKL KEIAFPRTDELKNDLLKKYNVE YQEYLQSKNKYKAEILKKLEHQ RLIEAERKRIAQMRQQQLESEQ FLFFEDQLKKQELARGQMRSQQ TSGLSEQIDGSALSCFSTHQNN SLLNVFADQPNKSDATNYASHS PPVNRALTPAATLSAVQNLVVE GLRCVVLPEDLCHKFLQLAESN TVRGIETCGILCGK LTHNEFTITHVIVPKQSAGPDY CDMENVEELFNVQDQHDLLTLG WIHTHPTQTAFLSSVDLHTHCS YQLMLPEAIAIVCSPKHKDTGI FRLTNAGMLEVSACKKKGFHPH TKEPRLFSICKHVLVKDIKIIV LDLR	214	VVLPEDLCHKFLQLAESNTV RGIETCGILCGKLTHNEFTI THVIVPKQSAGPDYCDMENV EELFNVQDQHDLLTLGWIHT HPTQTAFLSSVDLHTHCSYQ LMLPEAIAIVCSPKHKDTGI FRLTNAGMLEVSACKKKGFH PHTKEPRLFSICKHVLVKDI KIIVLDLR
CSN6_HUMAN COP9 signalosome complex subunit 6	107	MAAAAAAAAATNGTGGSSGMEV DAAVVPSVMACGVTGSVSVALH PLVILNISDHWIRMRSQEGRPV QVIGALIGKQEGRNIEVMNSFE LLSHTVEEKIIIDKEYYYTKEE QFKQVFKELEFLGWYTTGGPPD PSDIHVHKQVCEIIESPLFLKL NPMTKHTDLPVSVFESVIDIIN GEATMLFAELTYTLATEEAERI GVDHVARMTATGSGENSTVAEH LIAQHSAIKMLHSRVKLILEYV KASEAGEVPFNHEILREAYALC HCLPVLSTDKFKTDFYDQCNDV GLMAYLGTITKTCNTMNQFVNK FNVLYDRQGIGRRMRGLFF	215	VALHPLVILNISDHWIRMRS QEGRPVQVIGALIGKQEGRN IEVMNSFELLSHTVEEKIII DKEYYYTKEEQFKQVFKELE FLGWYTTGGPPDPSDIHVHK QVCEIIESPLFLKLNPMTKH TDLPVSVFESVIDIINGEAT MLFAELTYTLATEEAERIGV DHVARMTATGSGENSTVAEH LIAQHSAIKMLHSRVKLILE YVKASEAGEVPFNHEILREA YALCHCLPVLSTDKFKTDFY DQCNDVGLMAYLGTITKTCN TMNQFVNKFNVLYDRQGIGR RMRGLFF
EIF3F_HUMAN Eukaryotic translation initiation factor 3 subunit F	108	MATPAVPVSAPPATPTPVPAAA PASVPAPTPAPAAAPVPAAAPA SSSDPAAAAAATAAPGQTPASA QAPAQTPAPALPGPALPGPFPG GRVVRLHPVILASIVDSYERRN EGAARVIGTLLGTVDKHSVEVT NCFSVPHNESEDEVAVDMEFAK NMYELHKKVSPNELILGWYATG HDITEHSVLIHEYYSREAPNPI HLTVDTSLQNGRMSIKAYVSTL MGVPGRTMGVMFTPLTVKYAYY	216	VRLHPVILASIVDSYERRNE GAARVIGTLLGTVDKHSVEV TNCFSVPHNESEDEVAVDME FAKNMYELHKKVSPNELILG WYATGHDITEHSVLIHEYYS REAPNPIHLTVDTSLQNGRM SIKAYVSTLMGVPGRTMGVM FTPLTVKYAYYDTERIGVDL IMKTCFSPNRVIGLSSDLQQ VGGASARIQDALSTVLQYAE DVLSGKVSADNTVGRFLMSL

		DTERIGVDLIMKTCFSPNRVIG LSSDLQQVGGASARIQDALSTV LQYAEDVLSGKVSADNTVGRFL MSLVNQVPKIVPDDFETMLNSN INDLLMVTYLANLTQSQIALNE KLVNL		VNQVPKIVPDDFETMLNSNI NDLLMVTYLANLTQSQIALN EKLVNL
PSMD7_HUMAN 26S proteasome non-ATPase regulatory subunit 7	109	MPELAVQKVVVHPLVLLSVVDH FNRIGKVGNQKRVVGVLLGSWQ KKVLDVSNSFAVPFDEDDKDDS VWFLDHDYLENMYGMFKKVNAR ERIVGWYHTGPKLHKNDIAINE LMKRYCPNSVLVIIDVKPKDLG LPTEAYISVEEVHDDGTPTSKT FEHVTSEIGAEEAEEVGVEHLL RDIKDTTVGTLSQRITNQVHGL KGLNSKLLDIRSYLEKVATGKL PINHQIIYQLQDVFNLLPDVSL QEFVKAFYLKTNDQMVVVYLAS LIRSVVALHNLINNKIANRDAE KKEGQEKEESKKDRKEDKEKDK DKEKSDVKKEEKKEKK	217	VVVHPLVLLSVVDHFNRIGK VGNQKRVVGVLLGSWQKKVL DVSNSFAVPFDEDDKDDSVW FLDHDYLENMYGMFKKVNAR ERIVGWYHTGPKLHKNDIAI NELMKRYCPNSVLVIIDVKP KDLGLPTEAYISVEEVHDDG TPTSKTFEHVTSEIGAEEAE EVGVEHLLRDIKDTTVGTLS QRITNQVHGLKGLNSKLLDI RSYLEKVATGKLPINHQIIY QLQDVFNLLPDVSLQEFVKA FYLKTNDQMVVVYLASLIRS VVALHNLINNKIANRDAEKK EGQEKEESKKDRKEDKEKDK DKEKSDVKKEEKKEKK
EIF3H_HUMAN Eukaryotic translation initiation factor 3 subunit H	110	MASRKEGTGSTATSSSSTAGAA GKGKGKGGSGDSAVKQVQIDGL VVLKIIKHYQEEGQGTEVVQGV LLGLVVEDRLEITNCFPFPQHT EDDADFDEVQYQMEMMRSLRHV NIDHLHVGWYQSTYYGSFVTRA LLDSQFSYQHAIEESVVLIYDP IKTAQGSLSLKAYRLTPKLMEV CKEKDFSPEALKKANITFEYMF EEVPIVIKNSHLINVLMWELEK KSAVADKHELLSLASSNHLG KNLQLLMDRVDEMSQDIVKYNT YMRNTSKQQQQKHQYQQRRQQE NMQRQSRGEPPLPEEDLSKLFK PPQPPARMDSLLIAGQINTYCQ NIKEFTAQNLGKLFMAQALQEY NN	218	VQIDGLVVLKIIKHYQEEGQ GTEVVQGVLLGLVVEDRLEI TNCFPFPQHTEDDADFDEVQ YQMEMMRSLRHVNIDHLHVG WYQSTYYGSFVTRALLDSQF SYQHAIEESVVLIYDPIKTA QGSLSLKAYRLTPKLMEVCK EKDFSPEALKKANITFEYMF EEVPIVIKNSHLINVLMWEL EKKSAVADKHELLSLASSNH LGKNLQLLMDRVDEMSQDIV KYNTYMRNTSKQQQQKHQYQ QRRQQENMQRQSRGEPPLPE EDLSKLFKPPQPPARMDSLL IAGQINTYCQNIKEFTAQNL GKLFMAQALQEYNN
CSN5_HUMAN COP9 signalosome complex subunit 5	111	MAASGSGMAQKTWELANNMQEA QSIDEIYKYDKKQQQEILAAKP WTKDHHYFKYCKISALALLKMV MHARSGGNLEVMGLMLGKVDGE TMIIMDSFALPVEGTETRVNAQ AAAYEYMAAYIENAKQVGRLEN AIGWYHSHPGYGCWLSGIDVST QMLNQQFQEPFVAVVIDPTRTI SAGKVNLGAFRTYPKGYKPPDE GPSEYQTIPLNKIEDFGVHCKQ YYALEVSYFKSSLDRKLLELLW NKYWVNTLSSSSLLTNADYTTG	219	YCKISALALLKMVMHARSGG NLEVMGLMLGKVDGETMIIM DSFALPVEGTETRVNAQAAA YEYMAAYIENAKQVGRLENA IGWYHSHPGYGCWLSGIDVS TQMLNQQFQEPFVAVVIDPT RTISAGKVNLGAFRTYPKGY KPPDEGPSEYQTIPLNKIED FGVHCKQYYALEVSYFKSSL DRKLLELLWNKYWVNTLSSS SLLTNADYTTGQVFDLSEKL EQSEAQLGRGSFMLGLETHD

		QVFDLSEKLEQSEAQLGRGSFM LGLETHDRKSEDKLAKATRDSC KTTIEAIHGLMSQVIKDKLFNQ INIS		RKSEDKLAKATRDSCKTTIE AIHGLMSQVIKDKLFNQINI S
BRCC3_HU MAN Lys-63-specific deubiquitinase BRCC36	112	MAVQVVQAVQAVHLESDAFLVC LNHALSTEKEEVMGLCIGELND DTRSDSKFAYTGTEMRTVAEKV DAVRIVHIHSVIILRRSDKRKD RVEISPEQLSAASTEAERLAEL TGRPMRVVGWYHSHPHITVWPS HVDVRTQAMYQMMDQGFVGLIF SCFIEDKNTKTGRVLYTCFQSI QAQKSSESLHGPRDFWSSSQHI SIEGQKEEERYERIEIPIHIVP HVTIGKVCLESAVELPKILCQE EQDAYRRIHSLTHLDSVTKIHN GSVFTKNLCSQMSAVSGPLLQW LEDRLEQNQQHLQELQQEKEEL MQELSSLE	220	VHLESDAFLVCLNHALSTEK EEVMGLCIGELNDDTRSDSK FAYTGTEMRTVAEKVDAVRI VHIHSVIILRRSDKRKDRVE ISPEQLSAASTEAERLAELT GRPMRVVGWYHSHPHITVWP SHVDVRTQAMYQMMDQGFVG LIFSCFIEDKNTKTGRVLYT CFQSIQAQKSSESLHGPRDF WSSSQHISIEGQKEEERYER IEIPIHIVPHVTIGKVCLES AVELPKILCQEEQDAYRRIH SLTHLDSVTKIHNGSVFTKN LCSQMSAVSGPLLQWLEDRL EQNQQHLQELQQEKEELMQE LSSLE

5.3.2 Targeting Domain

[00213] In some embodiments, the targeting domain comprises a targeting moiety that specifically binds to a target membrane protein. In some embodiments, the targeting moiety comprises an antibody (or antigen binding fragment thereof). In some embodiments, the antibody is a full-length antibody, a single chain variable fragment (scFv), a $(scFv)_2$, a scFv-Fc, a Fab, a Fab', a $(Fab')_2$, a F(v), a single domain antibody, a single chain antibody, a VHH, or a $(VHH)_2$.. In some embodiments the targeting moiety comprises a VHH. In some embodiments the targeting moiety comprises a $(VHH)_2$.

[00214] In some embodiments, the targeting moiety specifically binds to a wild type target membrane protein. In some embodiments, the targeting moiety specifically binds to a wild type target membrane protein, but does not specifically binds to a variant of the target membrane protein associated with a genetic disease. In some embodiments, the targeting moiety specifically binds to a naturally occurring variant of a target membrane protein. In some embodiments, the targeting moiety specifically binds to a naturally occurring variant of a target membrane protein that is associated with a genetic disease (e.g., a genetic disease described herein). In some embodiments, the targeting moiety specifically binds to a naturally occurring variant of a target membrane protein that is a cause of a genetic disease (e.g., a genetic disease described herein). In some embodiments, the targeting moiety specifically binds a naturally occurring variant of a target membrane protein

that is a loss of a function variant. In some embodiments, the targeting moiety specifically binds a naturally occurring variant of a target membrane protein that is a loss of a function variant associated with a genetic disease (e.g., a genetic disease described herein). In some embodiments, the targeting moiety specifically binds a naturally occurring variant of a target membrane protein that is a loss of a function variant that causes a genetic disease (e.g., a genetic disease described herein).

5.3.2.1 Exemplary Target Membrane Proteins

[00215] In some embodiments, targeting moiety specifically binds a target membrane protein (e.g., a membrane protein described herein). Exemplary target membrane proteins include, but are not limited to, glutamate receptor ionotropic NMDA 2B (GRIN2B), cystic fibrosis transmembrane conductance regulator (CFTR), sodium channel protein type 1 subunit alpha (SCN1A), copper-transporting ATPase 2 (ATP7B), potassium voltage-gated channel subfamily KQT member 2 (KCNQ2), sodium channel protein type 2 subunit alpha (SCN2A), voltage-dependent P/Q-type calcium channel subunit alpha-1A (CACNA1A), solute carrier family 2, facilitated glucose transporter member 1 (SLC2A1), sodium channel protein type 8 subunit alpha (SCN8A), proline-rich transmembrane protein 2 (PRRT2), glutamate receptor ionotropic, NMDA 2A (GRIN2A), sodium- and chloride-dependent GABA transporter 1 (SLC6A1), usherin (USH2A), sodium/potassium-transporting ATPase subunit alpha-2 (ATP1A2), sodium/potassium-transporting ATPase subunit alpha-3 (ATP1A3), sodium channel protein type 9 subunit alpha (SCN9A), protocadherin-19 (PCDH19), gamma-aminobutyric acid receptor subunit beta-3 (GABRB3), tuberin (TSC2),hamartin (TSC1), potassium voltage-gated channel subfamily KQT member 3 (KCNQ3), dystrophin (DMD), rhodopsin (RHO), protein jagged-1 (JAG1), inositol 1,4,5-trisphosphate receptor type 1 (ITPR1), sugar transporter SWEET1 (SLC50A1), transmembrane protein 258 (TMEM258), and follicle-stimulating hormone receptor (FSHR).

[00216] In some embodiments, the target membrane protein is GRIN2B. In some embodiments, the target membrane protein is CFTR. In some embodiments, the target membrane protein is SCN1A. In some embodiments, the target membrane protein is ATP7B. In some embodiments, the target membrane protein is KCNQ2. In some embodiments, the target membrane protein is SCN2A. In some embodiments, the target membrane protein is CACNA1A. In some embodiments, the target membrane protein is SLC2A1. In some embodiments, the target membrane protein is SCN8A. In some embodiments, the target membrane protein is PRRT2. In

some embodiments, the target membrane protein is GRIN2A. In some embodiments, the target membrane protein is SLC6A1. In some embodiments, the target membrane protein is USH2A. In some embodiments, the target membrane protein is ATP1A2. In some embodiments, the target membrane protein is ATP1A3. In some embodiments, the target membrane protein is SCN9A. In some embodiments, the target membrane protein is PCDH19. In some embodiments, the target membrane protein is GABRB3. In some embodiments, the target membrane protein is TSC2. In some embodiments, the target membrane protein is TSC1. In some embodiments, the target membrane protein is KCNQ3. In some embodiments, the target membrane protein is DMD. In some embodiments, the target membrane protein is RHO. In some embodiments, the target membrane protein is JAG1. In some embodiments, the target membrane protein is ITPR1. In some embodiments, the target membrane protein is sugar transporter SWEET1 (SLC50A1). In some embodiments, the target membrane protein is transmembrane protein 258 (TMEM258). In some embodiments, the target membrane protein is follicle-stimulating hormone receptor (FSHR).

[00217] In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 221-245. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 221. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 222. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 223. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 224. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 225. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 226. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%

identical to the amino acid sequence of SEQ ID NO: 227. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 228. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 229. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 230. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 240. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 241. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 242. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 243. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 244. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 245. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 294. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 295. In some embodiments, the target membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 296.

[00218] Table 2 below, provides the wild type amino acid sequence of exemplary proteins to target for deubiquitination utilizing the fusion proteins described herein.

Table 2. The amino acid sequence of exemplary membrane proteins to target for deubiquitination utilizing the fusion proteins described herein and exemplary disease associations

Description	Disease Associations	SEQ ID NO	WT Amino Acid Sequence
Solute carrier family 2, facilitated glucose transporter member 1 (SLC2A1)	GLUT1 Deficiency Syndrome	221	MEPSSKKLTGRLMLAVGGAVLGSLQFGYNTGVINA PQKVIEEFYNQTWVHRYGESILPTTLTTLWSLSVA IFSVGGMIGSFSVGLFVNRFGRRNSMLMMNLLAFV SAVLMGFSKLGKSFEMLILGRFIIGVYCGLTTGFV PMYVGEVSPTALRGALGTLHQLGIVVGILIAQVFG LDSIMGNKDLWPLLLSIIFIPALLQCIVLPFCPES PRFLLINRNEENRAKSVLKKLRGTADVTHDLQEMK EESRQMMREKKVTILELFRSPAYRQPILIAVVLQL SQQLSGINAVFYYSTSIFEKAGVQQPVYATIGSGI VNTAFTVVSLFVVERAGRRTLHLIGLAGMAGCAIL MTIALALLEQLPWMSYLSIVAIFGFVAFFEVGPGP IPWFIVAELFSQGPRPAAIAVAGFSNWTSNFIVGM CFQYVEQLCGPYVFIIFTVLLVLFFIFTYFKVPET KGRTFDEIASGFRQGGASQSDKTPEELFHPLGADS QV
Proline-rich transmembrane protein 2 (PRRT2)	PRRT2 Dyskinesia & Epilepsy; Episodic kinesigenic dyskinesia 1	222	MAASSSEISEMKGVEESPKVPGEGPGHSEAETGPP QVLAGVPDQPEAPQPGPNTTAAPVDSGPKAGLAPE TTETPAGASETAQATDLSLSPGGESKANCSPEDPC QETVSKPEVSKEATADQGSRLESAAPPEPAPEPAP QPDPRPDSQPTPKPALQPELPTQEDPTPEILSESV GEKQENGAVVPLQAGDGEEGPAPEPHSPPSKKSPP ANGAPPRVLQQLVEEDRMRRAHSGHPGSPRGSLSR HPSSQLAGPGVEGGEGTQKPRDYIILAILSCFCPM WPVNIVAFAYAVMSRNSLQQGDVDGAQRLGRVAKL LSIVALVGGVLIIIASCVINLGVYK
Usherin (USH2A) Signal Sequence Underlined	Usher syndrome, type 2A	223	MNCPVLSLGSGFLFQVIEMLIFAYFASISLTESRG LFPRLENVGAFKKVSIVPTQAVCGLPDRSTFCHSS AAAESIQFCTQRFCIQDCPYRSSHPTYTALFSAGL SSCITPDKNDLHPNAHSNSASFIFGNHKSCFSSPP SPKLMASFTLAVWLKPEQQGVMCVIEKTVDGQIVF KLTISEKETMFYYRTVNGLQPPIKVMTLGRILVKK WIHLSVQVHQTKISFFINGVEKDHTPFNARTLSGS ITDFASGTVQIGQSLNGLEQFVGRMQDFRLYQVAL TNREILEVFSGDLLRLHAQSHCRCPGSHPRVHPLA QRYCIPNDAGDTADNRVSRLNPEAHPLSFVNDNDV GTSWVSNVFTNITQLNQGVTISVDLENGQYQVFYI IIQFFSPQPTEIRIQRKKENSLDWEDWQYFARNCG AFGMKNNGDLEKPDSVNCLQLSNFTPYSRGNVTFS ILTPGPNYRPGYNNFYNTPSLQEFVKATQIRFHFH GQYYTTETAVNLRHRYYAVDEITISGRCQCHGHAD NCDTTSQPYRCLCSQESFTEGLHCDRCLPLYNDKP FRQGDQVYAFNCKPCQCNSHSKSCHYNISVDPFPF EHFRGGGGVCDDCEHNTTGRNCELCKDYFFRQVGA DPSAIDVCKPCDCDTVGTRNGSILCDQIGGQCNCK RHVSGRQCNQCQNGFYNLQELDPDGCSPCNCNTSG TVDGDITCHQNSGQCKCKANVIGLRCDHCNFGFKF

			LRSFNDVGCEPCQCNLHGSVNKFCNPHSGQCECKK EAKGLQCDTCRENFYGLDVTNCKACDCDTAGSLPG TVCNAKTGQCICKPNVEGRQCNKCLEGNFYLRQNN SFLCLPCNCDKTGTINGSLLCNKSTGQCPCKLGVT GLRCNQCEPHRYNLTIDNFQHCQMCECDSLGTLPG TICDPISGQCLCVPNRQGRRCNQCQPGFYISPGNA TGCLPCSCHTTGAVNHICNSLTGQCVCQDASIAGQ RCDQCKDHYFGFDPQTGRCQPCNCHLSGALNETCH LVTGQCFCKQFVTGSKCDACVPSASHLDVNNLLGC SKTPFQQPPPRGQVQSSSAINLSWSPPDSPNAHWL TYSLLRDGFEIYTTEDQYPYSIQYFLDTDLLPYTK YSYYIETTNVHGSTRSVAVTYKTKPGVPEGNLTLS YIIPIGSDSVTLTWTTLSNQSGPIEKYILSCAPLA GGQPCVSYEGHETSATIWNLVPFAKYDFSVQACTS GGCLHSLPITVTTAQAPPQRLSPPKMQKISSTELH VEWSPPAELNGIIIRYELYMRRLRSTKETTSEESR VFQSSGWLSPHSFVESANENALKPPQTMTTITGLE PYTKYEFRVLAVNMAGSVSSAWVSERTGESAPVFM IPPSVFPLSSYSLNISWEKPADNVTRGKVVGYDIN MLSEQSPQQSIPMAFSQLLHTAKSQELSYTVEGLK PYRIYEFTITLCNSVGCVTSASGAGQTLAAAPAQL RPPLVKGINSTTIHLRWFPPEELNGPSPIYQLERR ESSLPALMTTMMKGIRFIGNGYCKFPSSTHPVNTD FTGIKASFRTKVPEGLIVFAASPGNQEEYFALQLK KGRLYFLFDPQGSPVEVTTTNDHGKQYSDGKWHEI IAIRHQAFGQITLDGIYTGSSAILNGSTVIGDNTG VFLGGLPRSYTILRKDPEIIQKGFVGCLKDVHFMK NYNPSAIWEPLDWQSSEEQINVYNSWEGCPASLNE GAQFLGAGFLELHPYMFHGGMNFEISFKFRTDQLN GLLLFVYNKDGPDFLAMELKSGILTFRLNTSLAFT QVDLLLGLSYCNGKWNKVIIKKEGSFISASVNGLM KHASESGDQPLVVNSPVYVGGIPQELLNSYQHLCL EQGFGGCMKDVKFTRGAVVNLASVSSGAVRVNLDG CLSTDSAVNCRGNDSILVYQGKEQSVYEGGLQPFT EYLYRVIASHEGGSVYSDWSRGRTTGAAPQSVPTP SRVRSLNGYSIEVTWDEPVVRGVIEKYILKAYSED STRPPRMPSASAEFVNTSNLTGILTGLLPFKNYAV TLTACTLAGCTESSHALNISTPQEAPQEVQPPVAK SLPSSLLLSWNPPKKANGIITQYCLYMDGRLIYSG SEENYIVTDLAVFTPHQFLLSACTHVGCTNSSWVL LYTAQLPPEHVDSPVLTVLDSRTIHIQWKQPRKIS GILERYVLYMSNHTHDFTIWSVIYNSTELFQDHML QYVLPGNKYLIKLGACTGGGCTVSEASEALTDEDI PEGVPAPKAHSYSPDSFNVSWTEPEYPNGVITSYG LYLDGILIHNSSELSYRAYGFAPWSLHSFRVQACT AKGCALGPLVENRTLEAPPEGTVNVFVKTQGSRKA HVRWEAPFRPNGLLTHSVLFTGIFYVDPVGNNYTL LNVTKVMYSGEETNLWVLIDGLVPFTNYTVQVNIS NSQGSLITDPITIAMPPGAPDGVLPPRLSSATPTS LQVVWSTPARNNAPGSPRYQLQMRSGDSTHGFLEL FSNPSASLSYEVSDLQPYTEYMFRLVASNGFGSAH

			SSWIPFMTAEDKPGPVVPPILLDVKSRMMLVTWQH PRKSNGVITHYNIYLHGRLYLRTPGNVTNCTVMHL HPYTAYKFQVEACTSKGCSLSPESQTVWTLPGAPE GIPSPELFSDTPTSVIISWQPPTHPNGLVENFTIE RRVKGKEEVTTLVTLPRSHSMRFIDKTSALSPWTK YEYRVLMSTLHGGTNSSAWVEVTTRPSRPAGVQPP VVTVLEPDAVQVTWKPPLIQNGDILSYEIHMPDPH ITLTNVTSAVLSQKVTHLIPFTNYSVTIVACSGGN GYLGGCTESLPTYVTTHPTVPQNVGPLSVIPLSES YVVISWQPPSKPNGPNLRYELLRRKIQQPLASNPP EDLNRWHNIYSGTQWLYEDKGLSRFTTYEYMLFVH NSVGFTPSREVTVTTLAGLPERGANLTASVLNHTA IDVRWAKPTVQDLQGEVEYYTLFWSSATSNDSLKI LPDVNSHVIGHLKPNTEYWIFISVFNGVHSINSAG LHATTCDGEPQGMLPPEVVIINSTAVRVIWTSPSN PNGVVTEYSIYVNNKLYKTGMNVPGSFILRDLSPF TIYDIQVEVCTIYACVKSNGTQITTVEDTPSDIPT PTIRGITSRSLQIDWVSPRKPNGIILGYDLLWKTW YPCAKTQKLVQDQSDELCKAVRCQKPESICGHICY SSEAKVCCNGVLYNPKPGHRCCEEKYIPFVLNSTG VCCGGRIQEAQPNHQCCSGYYARILPGEVCCPDEQ HNRVSVGIGDSCCGRMPYSTSGNQICCAGRLHDGH GQKCCGRQIVSNDLECCGGEEGVVYNRLPGMFCCG QDYVNMSDTICCSASSGESKAHIKKNDPVPVKCCE TELIPKSQKCCNGVGYNPLKYVCSDKISTGMMMKE TKECRILCPASMEATEHCGRCDFNFTSHICTVIRG SHNSTGKASIEEMCSSAEETIHTGSVNTYSYTDVN LKPYMTYEYRISAWNSYGRGLSKAVRARTKEDVPQ GVSPPTWTKIDNLEDTIVLNWRKPIQSNGPIIYYI LLRNGIERFRGTSLSFSDKEGIQPFQEYSYQLKAC TVAGCATSSKVVAATTQGVPESILPPSITALSAVA LHLSWSVPEKSNGVIKEYQIRQVGKGLIHTDTTDR RQHTVTGLQPYTNYSFTLTACTSAGCTSSEPFLGQ TLQAAPEGVWVTPRHIIINSTTVELYWSLPEKPNG LVSQYQLSRNGNLLFLGGSEEQNFTDKNLEPNSRY TYKLEVKTGGGSSASDDYIVQTPMSTPEEIYPPYN ITVIGPYSIFVAWIPPGILIPEIPVEYNVLLNDGS VTPLAFSVGHHQSTLLENLTPFTQYEIRIQACQNG SCGVSSRMFVKTPEAAPMDLNSPVLKALGSACIEI KWMPPEKPNGIIINYFIYRRPAGIEEESVLFVWSE GALEFMDEGDTLRPFTLYEYRVRACNSKGSVESLW SLTQTLEAPPQDFPAPWAQATSAHSVLLNWTKPES PNGIISHYRVVYQERPDDPTFNSPTVHAFTVKGTS HQAHLYGLEPFTTYRIGVVAANHAGEILSPWTLIQ TLESSPSGLRNFIVEQKENGRALLLQWSEPMRTNG VIKTYNIFSDGFLEYSGLNRQFLFRRLDPFTLYTL TLEACTRAGCAHSAPQPLWTDEAPPDSQLAPTVHS VKSTSVELSWSEPVNPNGKIIRYEVIRRCFEGKAW GNQTIQADEKIVFTEYNTERNTFMYNDTGLQPWTQ CEYKIYTWNSAGHTCSSWNVVRTLQAPPEGLSPPV ISYVSMNPQKLLISWIPPEQSNGIIQSYRLQRNEM

			LYPFSFDPVTFNYTDEELLPFSTYSYALQACTSGG CSTSKPTSITTLEAAPSEVSPPDLWAVSATQMNVC WSPPTVQNGKITKYLVRYDNKESLAGQGLCLLVSH LQPYSQYNFSLVACTNGGCTASVSKSAWTMEALPE NMDSPTLQVTGSESIEITWKPPRNPNGQIRSYELR RDGTIVYTGLETRYRDFTLTPGVEYSYTVTASNSQ GGILSPLVKDRTSPSAPSGMEPPKLQARGPQEILV NWDPPVRTNGDIINYTLFIRELFERETKIIHINTT HNSFGMQSYIVNQLKPFHRYEIRIQACTTLGCASS DWTFIQTPEIAPLMQPPPHLEVQMAPGGFQPTVSL LWTGPLQPNGKVLYYELYRRQIATQPRKSNPVLIY NGSSTSFIDSELLPFTEYEYQVWAVNSAGKAPSSW TWCRTGPAPPEGLRAPTFHVISSTQAVVNISAPGK PNGIVSLYRLFSSSAHGAETVLSEGMATQQTLHGL QAFTNYSIGVEACTCFNCCSKGPTAELRTHPAPPS GLSSPQIGTLASRTASFRWSPPMFPNGVIHSYELQ FHVACPPDSALPCTPSQIETKYTGLGQKASLGGLQ PYTTYKLRVVAHNEVGSTASEWISFTTQKELPQYR APFSVDSNLSVVCVNWSDTFLLNGQLKEYVLTDGG RRVYSGLDTTLYIPRTADKTFFFQVICTTDEGSVK TPLIQYDTSTGLGLVLTTPGKKKGSRSKSTEFYSE LWFIVLMAMLGLILLAIFLSLILQRKIHKEPYIRE RPPLVPLQKRMSPLNVYPPGENHMGLADTKIPRSG TPVSIRSNRSACVLRIPSQNQTSLTYSQGSLHRSV SQLMDIQDKKVLMDNSLWEAIMGHNSGLYVDEEDL MNAIKDFSSVTKERTTFTDTHL
Protocadherin-19 (PCDH19) Signal Sequence Underlined	PCDH19 Encephalopathy; Early Infantile Epileptic Encephalopathy 9	224	MESLLLPVLLLLAILWTQAAALINLKYSVEEEQRA GTVIANVAKDAREAGFALDPRQASAFRVVSNSAPH LVDINPSSGLLVTKQKIDRDLLCRQSPKCIISLEV MSSSMEICVIKVEIKDLNDNAPSFPAAQIELEISE AASPGTRIPLDSAYDPDSGSFGVQTYELTPNELFG LEIKTRGDGSRFAELVVEKSLDRETQSHYSFRITA LDGGDPPRLGTVGLSIKVTDSNDNNPVFSESTYAV SVPENSPPNTPVIRLNASDPDEGTNGQVVYSFYGY VNDRTRELFQIDPHSGLVTVTGALDYEEGHVYELD VQAKDLGPNSIPAHCKVTVSVLDTNDNPPVINLLS VNSELVEVSESAPPGYVIALVRVSDRDSGLNGRVQ CRLLGNVPFRLQEYESFSTILVDGRLDREQHDQYN LTIQARDGGVPMLQSAKSFTVLITDENDNHPHFSK PYYQVIVQENNTPGAYLLSVSARDPDLGLNGSVSY QIVPSQVRDMPVFTYVSINPNSGDIYALRSFNHEQ TKAFEFKVLAKDGGLPSLQSNATVRVIILDVNDNT PVITAPPLINGTAEVYIPRNSGIGYLVTVVKAEDY DEGENGRVTYDMTEGDRGFFEIDQVNGEVRTTRTF GESSKSSYELIVVAHDHGKTSLSASALVLIYLSPA LDAQESMGSVNLSLIFIIALGSIAGILFVTMIFVA IKCKRDNKEIRTYNCSNCLTITCLLGCFIKGQNSK CLHCISVSPISEEQDKKTEEKVSLRGKRIAEYSYG HQKKSSKKKKISKNDIRLVPRDVEETDKMNVVSCS SLTSSLNYFDYHQQTLPLGCRRSESTFLNVENQNT RNTSANHIYHHSFNSQGPQQPDLIINGVPLPETEN

			YSFDSNYVNSRAHLIKSSSTFKDLEGNSLKDSGHE ESDQTDSEHDVQRSLYCDTAVNDVLNTSVTSMGSQ MPDHDQNEGFHCREECRILGHSDRCWMPRNPMPIR SKSPEHVRNIIALSIEATAADVEAYDDCGPTKRTF ATFGKDVSDHPAEERPTLKGKRTVDVTICSPKVNS VIREAGNGCEAISPVTSPLHLKSSLPTKPSVSYTI ALAPPARDLEQYVNNVNNGPTRPSEAEPRGADSEK VMHEVSPILKEGRNKESPGVKRLKDIVL
Tuberin (TSC2)	Tuberous sclerosis-2	225	MAKPTSKDSGLKEKFKILLGLGTPRPNPRSAEGKQ TEFIITAEILRELSMECGLNNRIRMIGQICEVAKT KKFEEHAVEALWKAVADLLQPERPLEARHAVLALL KAIVQGQGERLGVLRALFFKVIKDYPSNEDLHERL EVFKALTDNGRHITYLEEELADFVLQWMDVGLSSE FLLVLVNLVKFNSCYLDEYIARMVQMICLLCVRTA SSVDIEVSLQVLDAVVCYNCLPAESLPLFIVTLCR TINVKELCEPCWKLMRNLLGTHLGHSAIYNMCHLM EDRAYMEDAPLLRGAVFFVGMALWGAHRLYSLRNS PTSVLPSFYQAMACPNEVVSYEIVLSITRLIKKYR KELQVVAWDILLNIIERLLQQLQTLDSPELRTIVH DLLTTVEELCDQNEFHGSQERYFELVERCADQRPE SSLLNLISYRAQSIHPAKDGWIQNLQALMERFFRS ESRGAVRIKVLDVLSFVLLINRQFYEEELINSVVI SQLSHIPEDKDHQVRKLATQLLVDLAEGCHTHHFN SLLDIIEKVMARSLSPPPELEERDVAAYSASLEDV KTAVLGLLVILQTKLYTLPASHATRVYEMLVSHIQ LHYKHSYTLPIASSIRLQAFDFLLLLRADSLHRLG LPNKDGVVRFSPYCVCDYMEPERGSEKKTSGPLSP PTGPPGPAPAGPAVRLGSVPYSLLFRVLLQCLKQE SDWKVLKLVLGRLPESLRYKVLIFTSPCSVDQLCS ALCSMLSGPKTLERLRGAPEGFSRTDLHLAVVPVL TALISYHNYLDKTKQREMVYCLEQGLIHRCASQCV VALSICSVEMPDIIIKALPVLVVKLTHISATASMA VPLLEFLSTLARLPHLYRNFAAEQYASVFAISLPY TNPSKFNQYIVCLAHHVIAMWFIRCRLPFRKDFVP FITKGLRSNVLLSFDDTPEKDSFRARSTSLNERPK SLRIARPPKQGLNNSPPVKEFKESSAAEAFRCRSI SVSEHVVRSRIQTSLTSASLGSADENSVAQADDSL KNLHLELTETCLDMMARYVFSNFTAVPKRSPVGEF LLAGGRTKTWLVGNKLVTVTTSVGTGTRSLLGLDS GELQSGPESSSSPGVHVRQTKEAPAKLESQAGQQV SRGARDRVRSMSGGHGLRVGALDVPASQFLGSATS PGPRTAPAAKPEKASAGTRVPVQEKTNLAAYVPLL TQGWAEILVRRPTGNTSWLMSLENPLSPFSSDINN MPLQELSNALMAAERFKEHRDTALYKSLSVPAAST AKPPPLPRSNTVASFSSLYQSSCQGQLHRSVSWAD SAVVMEEGSPGEVPVLVEPPGLEDVEAALGMDRRT DAYSRSSSVSSQEEKSLHAEELVGRGIPIERVVSS EGGRPSVDLSFQPSQPLSKSSSSPELQTLQDILGD PGDKADVGRLSPEVKARSQSGTLDGESAAWSASGE DSRGQPEGPLPSSSPRSPSGLRPRGYTISDSAPSR RGKRVERDALKSRATASNAEKVPGINPSFVFLQLY

			HSPFFGDESNKPILLPNESQSFERSVQLLDQIPSY DTHKIAVLYVGEGQSNSELAILSNEHGSYRYTEFL TGLGRLIELKDCQPDKVYLGGLDVCGEDGQFTYCW HDDIMQAVFHIATLMPTKDVDKHRCDKKRHLGNDF VSIVYNDSGEDFKLGTIKGQFNFVHVIVTPLDYEC NLVSLQCRKDMEGLVDTSVAKIVSDRNLPFVARQM ALHANMASQVHHSRSNPTDIYPSKWIARLRHIKRL RQRICEEAAYSNPSLPLVHPPSHSKAPAQTPAEPT PGYEVGQRKRLISSVEDFTEFV
Hamartin (TSC1)	Tuberous sclerosis-1	226	MAQQANVGELLAMLDSPMLGVRDDVTAVFKENLNS DRGPMLVNTLVDYYLETSSQPALHILTTLQEPHDK HLLDRINEYVGKAATRLSILSLLGHVIRLQPSWKH KLSQAPLLPSLLKCLKMDTDVVVLTTGVLVLITML PMIPQSGKQHLLDFFDIFGRLSSWCLKKPGHVAEV YLVHLHASVYALFHRLYGMYPCNFVSFLRSHYSMK ENLETFEEVVKPMMEHVRIHPELVTGSKDHELDPR RWKRLETHDVVIECAKISLDPTEASYEDGYSVSHQ ISARFPHRSADVTTSPYADTQNSYGCATSTPYSTS RLMLLNMPGQLPQTLSSPSTRLITEPPQATLWSPS MVCGMTTPPTSPGNVPPDLSHPYSKVFGTTAGGKG TPLGTPATSPPPAPLCHSDDYVHISLPQATVTPPR KEERMDSARPCLHRQHHLLNDRGSEEPPGSKGSVT LSDLPGFLGDLASEEDSIEKDKEEAAISRELSEIT TAEAEPVVPRGGFDSPFYRDSLPGSQRKTHSAASS SQGASVNPEPLHSSLDKLGPDTPKQAFTPIDLPCG SADESPAGDRECQTSLETSIFTPSPCKIPPPTRVG FGSGQPPPYDHLFEVALPKTAHHFVIRKTEELLKK AKGNTEEDGVPSTSPMEVLDRLIQQGADAHSKELN KLPLPSKSVDWTHFGGSPPSDEIRTLRDQLLLLHN QLLYERFKRQQHALRNRRLLRKVIKAAALEEHNAA MKDQLKLQEKDIQMWKVSLQKEQARYNQLQEQRDT MVTKLHSQIRQLQHDREEFYNQSQELQTKLEDCRN MIAELRIELKKANNKVCHTELLLSQVSQKLSNSES VQQQMEFLNRQLLVLGEVNELYLEQLQNKHSDTTK EVEMMKAAYRKELEKNRSHVLQQTQRLDTSQKRIL ELESHLAKKDHLLLEQKKYLEDVKLQARGQLQAAE SRYEAQKRITQVFELEILDLYGRLEKDGLLKKLEE EKAEAAEAAEERLDCCNDGCSDSMVGHNEEASGHN GETKTPRPSSARGSSGSRGGGGSSSSSSELSTPEK PPHQRAGPFSSRWETTMGEASASIPTTVGSLPSSK SFLGMKARELFRNKSESQCDEDGMTSSLSESLKTE LGKDLGVEAKIPLNLDGPHPSPPTPDSVGQLHIMD YNETHHEHS
Dystrophin (DMD)	Becker Muscular Dystrophy	227	MLWWEEVEDCYEREDVQKKTFTKWVNAQFSKFGKQ HIENLFSDLQDGRRLLDLLEGLTGQKLPKEKGSTR VHALNNVNKALRVLQNNNVDLVNIGSTDIVDGNHK LTLGLIWNIILHWQVKNVMKNIMAGLQQTNSEKIL LSWVRQSTRNYPQVNVINFTTSWSDGLALNALIHS HRPDLFDWNSVVCQQSATQRLEHAFNIARYQLGIE KLLDPEDVDTTYPDKKSILMYITSLFQVLPQQVSI EAIQEVEMLPRPPKVTKEEHFQLHHQMHYSQQITV

			SLAQGYERTSSPKPRFKSYAYTQAAYVTTSDPTRS PFPSQHLEAPEDKSFGSSLMESEVNLDRYQTALEE VLSWLLSAEDTLQAQGEISNDVEVVKDQFHTHEGY MMDLTAHQGRVGNILQLGSKLIGTGKLSEDEETEV QEQMNLLNSRWECLRVASMEKQSNLHRVLMDLQNQ KLKELNDWLTKTEERTRKMEEEPLGPDLEDLKRQV QQHKVLQEDLEQEQVRVNSLTHMVVVVDESSGDHA TAALEEQLKVLGDRWANICRWTEDRWVLLQDILLK WQRLTEEQCLFSAWLSEKEDAVNKIHTTGFKDQNE MLSSLQKLAVLKADLEKKKQSMGKLYSLKQDLLST LKNKSVTQKTEAWLDNFARCWDNLVQKLEKSTAQI SQAVTTTQPSLTQTTVMETVTTVTTREQILVKHAQ EELPPPPPQKKRQITVDSEIRKRLDVDITELHSWI TRSEAVLQSPEFAIFRKEGNFSDLKEKVNAIEREK AEKFRKLQDASRSAQALVEQMVNEGVNADSIKQAS EQLNSRWIEFCQLLSERLNWLEYQNNIIAFYNQLQ QLEQMTTTAENWLKIQPTTPSEPTAIKSQLKICKD EVNRLSDLQPQIERLKIQSIALKEKGQGPMFLDAD FVAFTNHFKQVFSDVQAREKELQTIFDTLPPMRYQ ETMSAIRTWVQQSETKLSIPQLSVTDYEIMEQRLG ELQALQSSLQEQQSGLYYLSTTVKEMSKKAPSEIS RKYQSEFEEIEGRWKKLSSQLVEHCQKLEEQMNKL RKIQNHIQTLKKWMAEVDVFLKEEWPALGDSEILK KQLKQCRLLVSDIQTIQPSLNSVNEGGQKIKNEAE PEFASRLETELKELNTQWDHMCQQVYARKEALKGG LEKTVSLQKDLSEMHEWMTQAEEEYLERDFEYKTP DELQKAVEEMKRAKEEAQQKEAKVKLLTESVNSVI AQAPPVAQEALKKELETLTTNYQWLCTRLNGKCKT LEEVWACWHELLSYLEKANKWLNEVEFKLKTTENI PGGAEEISEVLDSLENLMRHSEDNPNQIRILAQTL TDGGVMDELINEELETFNSRWRELHEEAVRRQKLL EQSIQSAQETEKSLHLIQESLTFIDKQLAAYIADK VDAAQMPQEAQKIQSDLTSHEISLEEMKKHNQGKE AAQRVLSQIDVAQKKLQDVSMKFRLFQKPANFEQR LQESKMILDEVKMHLPALETKSVEQEVVQSQLNHC VNLYKSLSEVKSEVEMVIKTGRQIVQKKQTENPKE LDERVTALKLHYNELGAKVTERKQQLEKCLKLSRK MRKEMNVLTEWLAATDMELTKRSAVEGMPSNLDSE VAWGKATQKEIEKQKVHLKSITEVGEALKTVLGKK ETLVEDKLSLLNSNWIAVTSRAEEWLNLLLEYQKH METFDQNVDHITKWIIQADTLLDESEKKKPQQKED VLKRLKAELNDIRPKVDSTRDQAANLMANRGDHCR KLVEPQISELNHRFAAISHRIKTGKASIPLKELEQ FNSDIQKLLEPLEAEIQQGVNLKEEDFNKDMNEDN EGTVKELLQRGDNLQQRITDERKREEIKIKQQLLQ TKHNALKDLRSQRRKKALEISHQWYQYKRQADDLL KCLDDIEKKLASLPEPRDERKIKEIDRELQKKKEE LNAVRRQAEGLSEDGAAMAVEPTQIQLSKRWREIE SKFAQFRRLNFAQIHTVREETMMVMTEDMPLEISY VPSTYLTEITHVSQALLEVEQLLNAPDLCAKDFED LFKQEESLKNIKDSLQQSSGRIDIIHSKKTAALQS

			ATPVERVKLQEALSQLDFQWEKVNKMYKDRQGRFD RSVEKWRRFHYDIKIFNQWLTEAEQFLRKTQIPEN WEHAKYKWYLKELQDGIGQRQTVVRTLNATGEEII QQSSKTDASILQEKLGSLNLRWQEVCKQLSDRKKR LEEQKNILSEFQRDLNEFVLWLEEADNIASIPLEP GKEQQLKEKLEQVKLLVEELPLRQGILKQLNETGG PVLVSAPISPEEQDKLENKLKQTNLQWIKVSRALP EKQGEIEAQIKDLGQLEKKLEDLEEQLNHLLLWLS PIRNQLEIYNQPNQEGPFDVKETEIAVQAKQPDVE EILSKGQHLYKEKPATQPVKRKLEDLSSEWKAVNR LLQELRAKQPDLAPGLTTIGASPTQTVTLVTQPVV TKETAISKLEMPSSLMLEVPALADFNRAWTELTDW LSLLDQVIKSQRVMVGDLEDINEMIIKQKATMQDL EQRRPQLEELITAAQNLKNKTSNQEARTIITDRIE RIQNQWDEVQEHLQNRRQQLNEMLKDSTQWLEAKE EAEQVLGQARAKLESWKEGPYTVDAIQKKITETKQ LAKDLRQWQTNVDVANDLALKLLRDYSADDTRKVH MITENINASWRSIHKRVSEREAALEETHRLLQQFP LDLEKFLAWLTEAETTANVLQDATRKERLLEDSKG VKELMKQWQDLQGEIEAHTDVYHNLDENSQKILRS LEGSDDAVLLQRRLDNMNFKWSELRKKSLNIRSHL EASSDQWKRLHLSLQELLVWLQLKDDELSRQAPIG GDFPAVQKQNDVHRAFKRELKTKEPVIMSTLETVR IFLTEQPLEGLEKLYQEPRELPPEERAQNVTRLLR KQAEEVNTEWEKLNLHSADWQRKIDETLERLQELQ EATDELDLKLRQAEVIKGSWQPVGDLLIDSLQDHL EKVKALRGEIAPLKENVSHVNDLARQLTTLGIQLS PYNLSTLEDLNTRWKLLQVAVEDRVRQLHEAHRDF GPASQHFLSTSVQGPWERAISPNKVPYYINHETQT TCWDHPKMTELYQSLADLNNVRFSAYRTAMKLRRL QKALCLDLLSLSAACDALDQHNLKQNDQPMDILQI INCLTTIYDRLEQEHNNLVNVPLCVDMCLNWLLNV YDTGRTGRIRVLSFKTGIISLCKAHLEDKYRYLFK QVASSTGFCDQRRLGLLLHDSIQIPRQLGEVASFG GSNIEPSVRSCFQFANNKPEIEAALFLDWMRLEPQ SMVWLPVLHRVAAAETAKHQAKCNICKECPIIGFR YRSLKHFNYDICQSCFFSGRVAKGHKMHYPMVEYC TPTTSGEDVRDFAKVLKNKFRTKRYFAKHPRMGYL PVQTVLEGDNMETPVTLINFWPVDSAPASSPQLSH DDTHSRIEHYASRLAEMENSNGSYLNDSISPNESI DDEHLLIQHYCQSLNQDSPLSQPRSPAQILISLES EERGELERILADLEEENRNLQAEYDRLKQQHEHKG LSPLPSPPEMMPTSPQSPRDAELIAEAKLLRQHKG RLEARMQILEDHNKQLESQLHRLRQLLEQPQAEAK VNGTTVSSPSTSLQRSDSSQPMLLRVVGSQTSDSM GEEDLLSPPQDTSTGLEEVMEQLNNSFPSSRGRNT PGKPMREDTM
Glutamate receptor ionotropic,	GRIN2B-Related Disorder;	228	MKPRAECCSPKFWLVLAVLAVSGSRARSQKSPPSI GIAVILVGTSDEVAIKDAHEKDDFHHLSVVPRVEL VAMNETDPKSIITRICDLMSDRKIQGVVFADDTDQ EAIAQILDFISAQTLTPILGIHGGSSMIMADKDES

NMDA 2B (GRIN2B) Signal Sequence Underlined	Epileptic encephalopathy, early infantile, 27		SMFFQFGPSIEQQASVMLNIMEEYDWYIFSIVTTY FPGYQDFVNKIRSTIENSFVGWELEEVLLLDMSLD DGDSKIQNQLKKLQSPIILLYCTKEEATYIFEVAN SVGLTGYGYTWIVPSLVAGDTDTVPAEFPTGLISV SYDEWDYGLPARVRDGIAIITTAASDMLSEHSFIP EPKSSCYNTHEKRIYQSNMLNRYLINVTFEGRNLS FSEDGYQMHPKLVIILLNKERKWERVGKWKDKSLQ MKYYVWPRMCPETEEQEDDHLSIVTLEEAPFVIVE SVDPLSGTCMRNTVPCQKRIVTENKTDEEPGYIKK CCKGFCIDILKKISKSVKFTYDLYLVTNGKHGKKI NGTWNGMIGEVVMKRAYMAVGSLTINEERSEVVDF SVPFIETGISVMVSRSNGTVSPSAFLEPFSADVWV MMFVMLLIVSAVAVFVFEYFSPVGYNRCLADGREP GGPSFTIGKAIWLLWGLVFNNSVPVQNPKGTTSKI MVSVWAFFAVIFLASYTANLAAFMIQEEYVDQVSG LSDKKFQRPNDFSPPFRFGTVPNGSTERNIRNNYA EMHAYMGKFNQRGVDDALLSLKTGKLDAFIYDAAV LNYMAGRDEGCKLVTIGSGKVFASTGYGIAIQKDS GWKRQVDLAILQLFGDGEMEELEALWLTGICHNEK NEVMSSQLDIDNMAGVFYMLGAAMALSLITFICEH LFYWQFRHCFMGVCSGKPGMVFSISRGIYSCIHGV AIEERQSVMNSPTATMNNTHSNILRLLRTAKNMAN LSGVNGSPQSALDFIRRESSVYDISEHRRSFTHSD CKSYNNPPCEENLFSDYISEVERTFGNLQLKDSNV YQDHYHHHHRPHSIGSASSIDGLYDCDNPPFTTQS RSISKKPLDIGLPSSKHSQLSDLYGKFSFKSDRYS GHDDLIRSDVSDISTHTVTYGNIEGNAAKRRKQQY KDSLKKRPASAKSRREFDEIELAYRRRPPRSPDHK RYFRDKEGLRDFYLDQFRTKENSPHWEHVDLTDIY KERSDDFKRDSVSGGGPCTNRSHIKHGTGDKHGVV SGVPAPWEKNLTNVEWEDRSGGNFCRSCPSKLHNY STTVTGQNSGRQACIRCEACKKAGNLYDISEDNSL QELDQPAAPVAVTSNASTTKYPQSPTNSKAQKKNR NKLRRQHSYDTFVDLQKEEAALAPRSVSLKDKGRF MDGSPYAHMFEMSAGESTFANNKSSVPTAGHHHHN NPGGGYMLSKSLYPDRVTQNPFIPTFGDDQCLLHG SKSYFFRQPTVAGASKARPDFRALVTNKPVVSALH GAVPARFQKDICIGNQSNPCVPNNKNPRAFNGSSN GHVYEKLSSIESDV
Cystic fibrosis transmembrane conductance regulator (CFTR)	Cystic fibrosis	229	MQRSPLEKASVVSKLFFSWTRPILRKGYRQRLELS DIYQIPSVDSADNLSEKLEREWDRELASKKNPKLI NALRRCFFWRFMFYGIFLYLGEVTKAVQPLLLGRI IASYDPDNKEERSIAIYLGIGLCLLFIVRTLLLHP AIFGLHHIGMQMRIAMFSLIYKKTLKLSSRVLDKI SIGQLVSLLSNNLNKFDEGLALAHFVWIAPLQVAL LMGLIWELLQASAFCGLGFLIVLALFQAGLGRMMM KYRDQRAGKISERLVITSEMIENIQSVKAYCWEEA MEKMIENLRQTELKLTRKAAYVRYFNSSAFFFSGF FVVFLSVLPYALIKGIILRKIFTTISFCIVLRMAV TRQFPWAVQTWYDSLGAINKIQDFLQKQEYKTLEY NLTTTEVVMENVTAFWEEGFGELFEKAKQNNNNRK

			TSNGDDSLFFSNFSLLGTPVLKDINFKIERGQLLA VAGSTGAGKTSLLMVIMGELEPSEGKIKHSGRISF CSQFSWIMPGTIKENIIFGVSYDEYRYRSVIKACQ LEEDISKFAEKDNIVLGEGGITLSGGQRARISLAR AVYKDADLYLLDSPFGYLDVLTEKEIFESCVCKLM ANKTRILVTSKMEHLKKADKILILHEGSSYFYGTF SELQNLQPDFSSKLMGCDSFDQFSAERRNSILTET LHRFSLEGDAPVSWTETKKQSFKQTGEFGEKRKNS ILNPINSIRKFSIVQKTPLQMNGIEEDSDEPLERR LSLVPDSEQGEAILPRISVISTGPTLQARRRQSVL NLMTHSVNQGQNIHRKTTASTRKVSLAPQANLTEL DIYSRRLSQETGLEISEEINEEDLKECFFDDMESI PAVTTWNTYLRYITVHKSLIFVLIWCLVIFLAEVA ASLVVLWLLGNTPLQDKGNSTHSRNNSYAVIITST SSYYVFYIYVGVADTLLAMGFFRGLPLVHTLITVS KILHHKMLHSVLQAPMSTLNTLKAGGILNRFSKDI AILDDLLPLTIFDFIQLLLIVIGAIAVVAVLQPYI FVATVPVIVAFIMLRAYFLQTSQQLKQLESEGRSP IFTHLVTSLKGLWTLRAFGRQPYFETLFHKALNLH TANWFLYLSTLRWFQMRIEMIFVIFFIAVTFISIL TTGEGEGRVGIILTLAMNIMSTLQWAVNSSIDVDS LMRSVSRVFKFIDMPTEGKPTKSTKPYKNGQLSKV MIIENSHVKKDDIWPSGGQMTVKDLTAKYTEGGNA ILENISFSISPGQRVGLLGRTGSGKSTLLSAFLRL LNTEGEIQIDGVSWDSITLQQWRKAFGVIPQKVFI FSGTFRKNLDPYEQWSDQEIWKVADEVGLRSVIEQ FPGKLDFVLVDGGCVLSHGHKQLMCLARSVLSKAK ILLLDEPSAHLDPVTYQIIRRTLKQAFADCTVILC EHRIEAMLECQQFLVIEENKVRQYDSIQKLLNERS LFRQAISPSDRVKLFPHRNSSKCKSKPQIAALKEE TEEEVQDTRL
Sodium channel protein type 1 subunit alpha (SCN1A)	Dravet syndrome	230	MEQTVLVPPGPDSFNFFTRESLAAIERRIAEEKAK NPKPDKKDDDENGPKPNSDLEAGKNLPFIYGDIPP EMVSEPLEDLDPYYINKKTFIVLNKGKAIFRFSAT SALYILTPFNPLRKIAIKILVHSLFSMLIMCTILT NCVFMTMSNPPDWTKNVEYTFTGIYTFESLIKIIA RGFCLEDFTFLRDPWNWLDFTVITFAYVTEFVDLG NVSALRTFRVLRALKTISVIPGLKTIVGALIQSVK KLSDVMILTVFCLSVFALIGLQLFMGNLRNKCIQW PPTNASLEEHSIEKNITVNYNGTLINETVFEFDWK SYIQDSRYHYFLEGFLDALLCGNSSDAGQCPEGYM CVKAGRNPNYGYTSFDTFSWAFLSLFRLMTQDFWE NLYQLTLRAAGKTYMIFFVLVIFLGSFYLINLILA VVAMAYEEQNQATLEEAEQKEAEFQQMIEQLKKQQ EAAQQAATATASEHSREPSAAGRLSDSSSEASKLS SKSAKERRNRRKKRKQKEQSGGEEKDEDEFQKSES EDSIRRKGFRFSIEGNRLTYEKRYSSPHQSLLSIR GSLFSPRRNSRTSLFSFRGRAKDVGSENDFADDEH STFEDNESRRDSLFVPRRHGERRNSNLSQTSRSSR MLAVFPANGKMHSTVDCNGVVSLVGGPSVPTSPVG QLLPEVIIDKPATDDNGTTTETEMRKRRSSSFHVS

			MDFLEDPSQRQRAMSIASILTNTVEELEESRQKCP PCWYKFSNIFLIWDCSPYWLKVKHVVNLVVMDPFV DLAITICIVLNTLFMAMEHYPMTDHFNNVLTVGNL VFTGIFTAEMFLKIIAMDPYYYFQEGWNIFDGFIV TLSLVELGLANVEGLSVLRSFRLLRVFKLAKSWPT LNMLIKIIGNSVGALGNLTLVLAIIVFIFAVVGMQ LFGKSYKDCVCKIASDCQLPRWHMNDFFHSFLIVF RVLCGEWIETMWDCMEVAGQAMCLTVFMMVMVIGN LVVLNLFLALLLSSFSADNLAATDDDNEMNNLQIA VDRMHKGVAYVKRKIYEFIQQSFIRKQKILDEIKP LDDLNNKKDSCMSNHTAEIGKDLDYLKDVNGTTSG IGTGSSVEKYIIDESDYMSFINNPSLTVTVPIAVG ESDFENLNTEDFSSESDLEESKEKLNESSSSSEGS TVDIGAPVEEQPVVEPEETLEPEACFTEGCVQRFK CCQINVEEGRGKQWWNLRRTCFRIVEHNWFETFIV FMILLSSGALAFEDIYIDQRKTIKTMLEYADKVFT YIFILEMLLKWVAYGYQTYFTNAWCWLDFLIVDVS LVSLTANALGYSELGAIKSLRTLRALRPLRALSRF EGMRVVVNALLGAIPSIMNVLLVCLIFWLIFSIMG VNLFAGKFYHCINTTTGDRFDIEDVNNHTDCLKLI ERNETARWKNVKVNFDNVGFGYLSLLQVATFKGWM DIMYAAVDSRNVELQPKYEESLYMYLYFVIFIIFG SFFTLNLFIGVIIDNFNQQKKKFGGQDIFMTEEQK KYYNAMKKLGSKKPQKPIPRPGNKFQGMVFDFVTR QVFDISIMILICLNMVTMMVETDDQSEYVTTILSR INLVFIVLFTGECVLKLISLRHYYFTIGWNIFDFV VVILSIVGMFLAELIEKYFVSPTLFRVIRLARIGR ILRLIKGAKGIRTLLFALMMSLPALFNIGLLLFLV MFIYAIFGMSNFAYVKREVGIDDMFNFETFGNSMI CLFQITTSAGWDGLLAPILNSKPPDCDPNKVNPGS SVKGDCGNPSVGIFFFVSYIIISFLVVVNMYIAVI LENFSVATEESAEPLSEDDFEMFYEVWEKFDPDAT QFMEFEKLSQFAAALEPPLNLPQPNKLQLIAMDLP MVSGDRIHCLDILFAFTKRVLGESGEMDALRIQME ERFMASNPSKVSYQPITTTLKRKQEEVSAVIIQRA YRRHLLKRTVKQASFTYNKNKIKGGANLLIKEDMI IDRINENSITEKTDLTMSTAACPPSYDRVTKPIVE KHEQEGKDEKAKGK
Copper-transporting ATPase 2 (ATP7B)	Wilson disease	231	MPEQERQITAREGASRKILSKLSLPTRAWEPAMKK SFAFDNVGYEGGLDGLGPSSQVATSTVRILGMTCQ SCVKSIEDRISNLKGIISMKVSLEQGSATVKYVPS VVCLQQVCHQIGDMGFEASIAEGKAASWPSRSLPA QEAVVKLRVEGMTCQSCVSSIEGKVRKLQGVVRVK VSLSNQEAVITYQPYLIQPEDLRDHVNDMGFEAAI KSKVAPLSLGPIDIERLQSTNPKRPLSSANQNFNN SETLGHQGSHVVTLQLRIDGMHCKSCVLNIEENIG QLLGVQSIQVSLENKTAQVKYDPSCTSPVALQRAI EALPPGNFKVSLPDGAEGSGTDHRSSSSHSPGSPP RNQVQGTCSTTLIAIAGMTCASCVHSIEGMISQLE GVQQISVSLAEGTATVLYNPSVISPEELRAAIEDM GFEASVVSESCSTNPLGNHSAGNSMVQTTDGTPTS

			VQEVAPHTGRLPANHAPDILAKSPQSTRAVAPQKC FLQIKGMTCASCVSNIERNLQKEAGVLSVLVALMA GKAEIKYDPEVIQPLEIAQFIQDLGFEAAVMEDYA GSDGNIELTITGMTCASCVHNIESKLTRTNGITYA SVALATSKALVKFDPEIIGPRDIIKIIEEIGFHAS LAQRNPNAHHLDHKMEIKQWKKSFLCSLVFGIPVM ALMIYMLIPSNEPHQSMVLDHNIIPGLSILNLIFF ILCTFVQLLGGWYFYVQAYKSLRHRSANMDVLIVL ATSIAYVYSLVILVVAVAEKAERSPVTFFDTPPML FVFIALGRWLEHLAKSKTSEALAKLMSLQATEATV VTLGEDNLIIREEQVPMELVQRGDIVKVVPGGKFP VDGKVLEGNTMADESLITGEAMPVTKKPGSTVIAG SINAHGSVLIKATHVGNDTTLAQIVKLVEEAQMSK APIQQLADRFSGYFVPFIIIMSTLTLVVWIVIGFI DFGVVQRYFPNPNKHISQTEVIIRFAFQTSITVLC IACPCSLGLATPTAVMVGTGVAAQNGILIKGGKPL EMAHKIKTVMFDKTGTITHGVPRVMRVLLLGDVAT LPLRKVLAVVGTAEASSEHPLGVAVTKYCKEELGT ETLGYCTDFQAVPGCGIGCKVSNVEGILAHSERPL SAPASHLNEAGSLPAEKDAVPQTFSVLIGNREWLR RNGLTISSDVSDAMTDHEMKGQTAILVAIDGVLCG MIAIADAVKQEAALAVHTLQSMGVDVVLITGDNRK TARAIATQVGINKVFAEVLPSHKVAKVQELQNKGK KVAMVGDGVNDSPALAQADMGVAIGTGTDVAIEAA DVVLIRNDLLDVVASIHLSKRTVRRIRINLVLALI YNLVGIPIAAGVFMPIGIVLQPWMGSAAMAASSVS VVLSSLQLKCYKKPDLERYEAQAHGHMKPLTASQV SVHIGMDDRWRDSPRATPWDQVSYVSQVSLSSLTS DKPSRHSAAADDDGDKWSLLLNGRDEEQYI
Potassium voltage-gated channel subfamily KQT member 2 (KCNQ2)	KCNQ2-Related Disorders (Epileptic Encephalopathy)	232	MVQKSRNGGVYPGPSGEKKLKVGFVGLDPGAPDST RDGALLIAGSEAPKRGSILSKPRAGGAGAGKPPKR NAFYRKLQNFLYNVLERPRGWAFIYHAYVFLLVFS CLVLSVFSTIKEYEKSSEGALYILEIVTIVVFGVE YFVRIWAAGCCCRYRGWRGRLKFARKPFCVIDIMV LIASIAVLAAGSQGNVFATSALRSLRFLQILRMIR MDRRGGTWKLLGSVVYAHSKELVTAWYIGFLCLIL ASFLVYLAEKGENDHFDTYADALWWGLITLTTIGY GDKYPQTWNGRLLAATFTLIGVSFFALPAGILGSG FALKVQEQHRQKHFEKRRNPAAGLIQSAWRFYATN LSRTDLHSTWQYYERTVTVPMYSSQTQTYGASRLI PPLNQLELLRNLKSKSGLAFRKDPPPEPSPSKGSP CRGPLCGCCPGRSSQKVSLKDRVFSSPRGVAAKGK GSPQAQTVRRSPSADQSLEDSPSKVPKSWSFGDRS RARQAFRIKGAASRQNSEEASLPGEDIVDDKSCPC EFVTEDLTPGLKVSIRAVCVMRFLVSKRKFKESLR PYDVMDVIEQYSAGHLDMLSRIKSLQSRVDQIVGR GPAITDKDRTKGPAEAELPEDPSMMGRLGKVEKQV LSMEKKLDFLVNIYMQRMGIPPTETEAYFGAKEPE PAPPYHSPEDSREHVDRHGCIVKIVRSSSSTGQKN FSAPPAAPPVQCPPSTSWQPQSHPRQGHGTSPVGD HGSLVRIPPPPAHERSLSAYGGGNRASMEFLRQED

			TPGCRPPEGNLRDSDTSISIPSVDHEELERSFSGF SISQSKENLDALNSCYAAVAPCAKVRPYIAEGESD TDSDLCTPCGPPPRSATGEGPFGDVGWAGPRK
Sodium channel protein type 2 subunit alpha (SCN2A)	SCN2A-Related Disorders; Epileptic encephalopathy, early infantile, 11	233	MAQSVLVPPGPDSFRFFTRESLAAIEQRIAEEKAK RPKQERKDEDDENGPKPNSDLEAGKSLPFIYGDIP PEMVSVPLEDLDPYYINKKTFIVLNKGKAISRFSA TPALYILTPFNPIRKLAIKILVHSLFNMLIMCTIL TNCVFMTMSNPPDWTKNVEYTFTGIYTFESLIKIL ARGFCLEDFTFLRDPWNWLDFTVITFAYVTEFVDL GNVSALRTFRVLRALKTISVIPGLKTIVGALIQSV KKLSDVMILTVFCLSVFALIGLQLFMGNLRNKCLQ WPPDNSSFEINITSFFNNSLDGNGTTFNRTVSIFN WDEYIEDKSHFYFLEGQNDALLCGNSSDAGQCPEG YICVKAGRNPNYGYTSFDTFSWAFLSLFRLMTQDF WENLYQLTLRAAGKTYMIFFVLVIFLGSFYLINLI LAVVAMAYEEQNQATLEEAEQKEAEFQQMLEQLKK QQEEAQAAAAAASAESRDFSGAGGIGVFSESSSVA SKLSSKSEKELKNRRKKKKQKEQSGEEEKNDRVRK SESEDSIRRKGFRFSLEGSRLTYEKRFSSPHQSLL SIRGSLFSPRRNSRASLFSFRGRAKDIGSENDFAD DEHSTFEDNDSRRDSLFVPHRHGERRHSNVSQASR ASRVLPILPMNGKMHSAVDCNGVVSLVGGPSTLTS AGQLLPEGTTTETEIRKRRSSSYHVSMDLLEDPTS RQRAMSIASILTNTMEELEESRQKCPPCWYKFANM CLIWDCCKPWLKVKHLVNLVVMDPFVDLAITICIV LNTLFMAMEHYPMTEQFSSVLSVGNLVFTGIFTAE MFLKIIAMDPYYYFQEGWNIFDGFIVSLSLMELGL ANVEGLSVLRSFRLLRVFKLAKSWPTLNMLIKIIG NSVGALGNLTLVLAIIVFIFAVVGMQLFGKSYKEC VCKISNDCELPRWHMHDFFHSFLIVFRVLCGEWIE TMWDCMEVAGQTMCLTVFMMVMVIGNLVVLNLFLA LLLSSFSSDNLAATDDDNEMNNLQIAVGRMQKGID FVKRKIREFIQKAFVRKQKALDEIKPLEDLNNKKD SCISNHTTIEIGKDLNYLKDGNGTTSGIGSSVEKY VVDESDYMSFINNPSLTVTVPIAVGESDFENLNTE EFSSESDMEESKEKLNATSSSEGSTVDIGAPAEGE QPEVEPEESLEPEACFTEDCVRKFKCCQISIEEGK GKLWWNLRKTCYKIVEHNWFETFIVFMILLSSGAL AFEDIYIEQRKTIKTMLEYADKVFTYIFILEMLLK WVAYGFQVYFTNAWCWLDFLIVDVSLVSLTANALG YSELGAIKSLRTLRALRPLRALSRFEGMRVVVNAL LGAIPSIMNVLLVCLIFWLIFSIMGVNLFAGKFYH CINYTTGEMFDVSVVNNYSECKALIESNQTARWKN VKVNFDNVGLGYLSLLQVATFKGWMDIMYAAVDSR NVELQPKYEDNLYMYLYFVIFIIFGSFFTLNLFIG VIIDNFNQQKKKFGGQDIFMTEEQKKYYNAMKKLG SKKPQKPIPRPANKFQGMVFDFVTKQVFDISIMIL ICLNMVTMMVETDDQSQEMTNILYWINLVFIVLFT GECVLKLISLRYYYFTIGWNIFDFVVVILSIVGMF LAELIEKYFVSPTLFRVIRLARIGRILRLIKGAKG IRTLLFALMMSLPALFNIGLLLFLVMFIYAIFGMS

			NFAYVKREVGIDDMFNFETFGNSMICLFQITTSAG WDGLLAPILNSGPPDCDPDKDHPGSSVKGDCGNPS VGIFFFVSYIIISFLVVVNMYIAVILENFSVATEE SAEPLSEDDFEMFYEVWEKFDPDATQFIEFAKLSD FADALDPPLLIAKPNKVQLIAMDLPMVSGDRIHCL DILFAFTKRVLGESGEMDALRIQMEERFMASNPSK VSYEPITTTLKRKQEEVSAIIIQRAYRRYLLKQKV KKVSSIYKKDKGKECDGTPIKEDTLIDKLNENSTP EKTDMTPSTTSPPSYDSVTKPEKEKFEKDKSEKED KGKDIRESKK
Voltage-dependent P/Q-type calcium channel subunit alpha-1A (CACNA1A)	CACNA1A-Related Disorders; Episodic ataxia, type 2	234	MARFGDEMPARYGGGGSGAAAGVVVGSGGGRGAGG SRQGGQPGAQRMYKQSMAQRARTMALYNPIPVRQN CLTVNRSLFLFSEDNVVRKYAKKITEWPPFEYMIL ATIIANCIVLALEQHLPDDDKTPMSERLDDTEPYF IGIFCFEAGIKIIALGFAFHKGSYLRNGWNVMDFV VVLTGILATVGTEFDLRTLRAVRVLRPLKLVSGIP SLQVVLKSIMKAMIPLLQIGLLLFFAILIFAIIGL EFYMGKFHTTCFEEGTDDIQGESPAPCGTEEPART CPNGTKCQPYWEGPNNGITQFDNILFAVLTVFQCI TMEGWTDLLYNSNDASGNTWNWLYFIPLIIIGSFF MLNLVLGVLSGEFAKERERVENRRAFLKLRRQQQI ERELNGYMEWISKAEEVILAEDETDGEQRHPFDAL RRTTIKKSKTDLLNPEEAEDQLADIASVGSPFARA SIKSAKLENSTFFHKKERRMRFYIRRMVKTQAFYW TVLSLVALNTLCVAIVHYNQPEWLSDFLYYAEFIF LGLFMSEMFIKMYGLGTRPYFHSSFNCFDCGVIIG SIFEVIWAVIKPGTSFGISVLRALRLLRIFKVTKY WASLRNLVVSLLNSMKSIISLLFLLFLFIVVFALL GMQLFGGQFNFDEGTPPTNFDTFPAAIMTVFQILT GEDWNEVMYDGIKSQGGVQGGMVFSIYFIVLTLFG NYTLLNVFLAIAVDNLANAQELTKDEQEEEEAANQ KLALQKAKEVAEVSPLSAANMSIAVKEQQKNQKPA KSVWEQRTSEMRKQNLLASREALYNEMDPDERWKA AYTRHLRPDMKTHLDRPLVVDPQENRNNNTNKSRA AEPTVDQRLGQQRAEDFLRKQARYHDRARDPSGSA GLDARRPWAGSQEAELSREGPYGRESDHHAREGSL EQPGFWEGEAERGKAGDPHRRHVHRQGGSRESRSG SPRTGADGEHRRHRAHRRPGEEGPEDKAERRARHR EGSRPARGGEGEGEGPDGGERRRRHRHGAPATYEG DARREDKERRHRRRKENQGSGVPVSGPNLSTTRPI QQDLGRQDPPLAEDIDNMKNNKLATAESAAPHGSL GHAGLPQSPAKMGNSTDPGPMLAIPAMATNPQNAA SRRTPNNPGNPSNPGPPKTPENSLIVTNPSGTQTN SAKTARKPDHTTVDIPPACPPPLNHTVVQVNKNAN PDPLPKKEEEKKEEEEDDRGEDGPKPMPPYSSMFI LSTTNPLRRLCHYILNLRYFEMCILMVIAMSSIAL AAEDPVQPNAPRNNVLRYFDYVFTGVFTFEMVIKM IDLGLVLHQGAYFRDLWNILDFIVVSGALVAFAFT GNSKGKDINTIKSLRVLRVLRPLKTIKRLPKLKAV FDCVVNSLKNVFNILIVYMLFMFIFAVVAVQLFKG KFFHCTDESKEFEKDCRGKYLLYEKNEVKARDREW

			KKYEFHYDNVLWALLTLFTVSTGEGWPQVLKHSVD ATFENQGPSPGYRMEMSIFYVVYFVVFPFFFVNIF VALIIITFQEQGDKMMEEYSLEKNERACIDFAISA KPLTRHMPQNKQSFQYRMWQFVVSPPFEYTIMAMI ALNTIVLMMKFYGASVAYENALRVFNIVFTSLFSL ECVLKVMAFGILNYFRDAWNIFDFVTVLGSITDIL VTEFGNNFINLSFLRLFRAARLIKLLRQGYTIRIL LWTFVQSFKALPYVCLLIAMLFFIYAIIGMQVFGN IGIDVEDEDSDEDEFQITEHNNFRTFFQALMLLFR SATGEAWHNIMLSCLSGKPCDKNSGILTRECGNEF AYFYFVSFIFLCSFLMLNLFVAVIMDNFEYLTRDS SILGPHHLDEYVRVWAEYDPAAWGRMPYLDMYQML RHMSPPLGLGKKCPARVAYKRLLRMDLPVADDNTV HFNSTLMALIRTALDIKIAKGGADKQQMDAELRKE MMAIWPNLSQKTLDLLVTPHKSTDLTVGKIYAAMM IMEYYRQSKAKKLQAMREEQDRTPLMFQRMEPPSP TQEGGPGQNALPSTQLDPGGALMAHESGLKESPSW VTQRAQEMFQKTGTWSPEQGPPTDMPNSQPNSQSV EMREMGRDGYSDSEHYLPMEGQGRAASMPRLPAEN QRRRGRPRGNNLSTISDTSPMKRSASVLGPKARRL DDYSLERVPPEENQRHHQRRRDRSHRASERSLGRY TDVDTGLGTDLSMTTQSGDLPSKERDQERGRPKDR KHRQHHHHHHHHHPPPPDKDRYAQERPDHGRARA RDQRWSRSPSEGREHMAHRQGSSSVSGSPAPSTSG TSTPRRGRRQLPQTPSTPRPHVSYSPVIRKAGGSG PPQQQQQQQQQQQQQAVARPGRAATSGPRRYPGPT AEPLAGDRPPTGGHSSGRSPRMERRVPGPARSESP RACRHGGARWPASGPHVSEGPPGPRHHGYYRGSDY DEADGPGSGGGEEAMAGAYDAPPPVRHASSGATGR SPRTPRASGPACASPSRHGRRLPNGYYPAHGLARP RGPGSRKGLHEPYSESDDDWC
Sodium channel protein type 8 subunit alpha (SCN8A)	SCN8A-Related Disorders; Epileptic encephalopathy, early infantile, 13	235	MAARLLAPPGPDSFKPFTPESLANIERRIAESKLK KPPKADGSHREDDEDSKPKPNSDLEAGKSLPFIYG DIPQGLVAVPLEDFDPYYLTQKTFVVLNRGKTLFR FSATPALYILSPFNLIRRIAIKILIHSVFSMIIMC TILTNCVFMTFSNPPDWSKNVEYTFTGIYTFESLV KIIARGFCIDGFTFLRDPWNWLDFSVIMMAYITEF VNLGNVSALRTFRVLRALKTISVIPGLKTIVGALI QSVKKLSDVMILTVFCLSVFALIGLQLFMGNLRNK CVVWPINFNESYLENGTKGFDWEEYINNKTNFYTV PGMLEPLLCGNSSDAGQCPEGYQCMKAGRNPNYGY TSFDTFSWAFLALFRLMTQDYWENLYQLTLRAAGK TYMIFFVLVIFVGSFYLVNLILAVVAMAYEEQNQA TLEEAEQKEAEFKAMLEQLKKQQEEAQAAAMATSA GTVSEDAIEEEGEEGGGSPRSSSEISKLSSKSAKE RRNRRKKRKQKELSEGEEKGDPEKVFKSESEDGMR RKAFRLPDNRIGRKFSIMNQSLLSIPGSPFLSRHN SKSSIFSFRGPGRFRDPGSENEFADDEHSTVEESE GRRDSLFIPIRARERRSSYSGYSGYSQGSRSSRIF PSLRRSVKRNSTVDCNGVVSLIGGPGSHIGGRLLP EATTEVEIKKKGPGSLLVSMDQLASYGRKDRINSI

			MSVVTNTLVEELEESQRKCPPCWYKFANTFLIWEC HPYWIKLKEIVNLIVMDPFVDLAITICIVLNTLFM AMEHHPMTPQFEHVLAVGNLVFTGIFTAEMFLKLI AMDPYYYFQEGWNIFDGFIVSLSLMELSLADVEGL SVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGAL GNLTLVLAIIVFIFAVVGMQLFGKSYKECVCKINQ DCELPRWHMHDFFHSFLIVFRVLCGEWIETMWDCM EVAGQAMCLIVFMMVMVIGNLVVLNLFLALLLSSF SADNLAATDDDGEMNNLQISVIRIKKGVAWTKLKV HAFMQAHFKQREADEVKPLDELYEKKANCIANHTG ADIHRNGDFQKNGNGTTSGIGSSVEKYIIDEDHMS FINNPNLTVRVPIAVGESDFENLNTEDVSSESDPE GSKDKLDDTSSSEGSTIDIKPEVEEVPVEQPEEYL DPDACFTEGCVQRFKCCQVNIEEGLGKSWWILRKT CFLIVEHNWFETFIIFMILLSSGALAFEDIYIEQR KTIRTILEYADKVFTYIFILEMLLKWTAYGFVKFF TNAWCWLDFLIVAVSLVSLIANALGYSELGAIKSL RTLRALRPLRALSRFEGMRVVVNALVGAIPSIMNV LLVCLIFWLIFSIMGVNLFAGKYHYCFNETSEIRF EIEDVNNKTECEKLMEGNNTEIRWKNVKINFDNVG AGYLALLQVATFKGWMDIMYAAVDSRKPDEQPKYE DNIYMYIYFVIFIIFGSFFTLNLFIGVIIDNFNQQ KKKFGGQDIFMTEEQKKYYNAMKKLGSKKPQKPIP RPLNKIQGIVFDFVTQQAFDIVIMMLICLNMVTMM VETDTQSKQMENILYWINLVFVIFFTCECVLKMFA LRHYYFTIGWNIFDFVVVILSIVGMFLADIIEKYF VSPTLFRVIRLARIGRILRLIKGAKGIRTLLFALM MSLPALFNIGLLLFLVMFIFSIFGMSNFAYVKHEA GIDDMFNFETFGNSMICLFQITTSAGWDGLLLPIL NRPPDCSLDKEHPGSGFKGDCGNPSVGIFFFVSYI IISFLIVVNMYIAIILENFSVATEESADPLSEDDF ETFYEIWEKFDPDATQFIEYCKLADFADALEHPLR VPKPNTIELIAMDLPMVSGDRIHCLDILFAFTKRV LGDSGELDILRQQMEERFVASNPSKVSYEPITTTL RRKQEEVSAVVLQRAYRGHLARRGFICKKTTSNKL ENGGTHREKKESTPSTASLPSYDSVTKPEKEKQQR AEEGRRERAKRQKEVRESKC
Glutamate receptor ionotropic, NMDA 2A (GRIN2A) Signal Sequence Underlined	GRIN2A-Related Disorder; Epilepsy, focal, with speech disorder and with or without mental retardation	236	MGRVGYWTLLVLPALLVWRGPAPSAAAEKGPPALN IAVMLGHSHDVTERELRTLWGPEQAAGLPLDVNVV ALLMNRTDPKSLITHVCDLMSGARIHGLVFGDDTD QEAVAQMLDFISSHTFVPILGIHGGASMIMADKDP TSTFFQFGASIQQQATVMLKIMQDYDWHVFSLVTT IFPGYREFISFVKTTVDNSFVGWDMQNVITLDTSF EDAKTQVQLKKIHSSVILLYCSKDEAVLILSEARS LGLTGYDFFWIVPSLVSGNTELIPKEFPSGLISVS YDDWDYSLEARVRDGIGILTTAASSMLEKFSYIPE AKASCYGQMERPEVPMHTLHPFMVNVTWDGKDLSF TEEGYQVHPRLVVIVLNKDREWEKVGKWENHTLSL RHAVWPRYKSFSDCEPDDNHLSIVTLEEAPFVIVE DIDPLTETCVRNTVPCRKFVKINNSTNEGMNVKKC CKGFCIDILKKLSRTVKFTYDLYLVTNGKHGKKVN

			NVWNGMIGEVVYQRAVMAVGSLTINEERSEVVDFS VPFVETGISVMVSRSNGTVSPSAFLEPFSASVWVM MFVMLLIVSAIAVFVFEYFSPVGYNRNLAKGKAPH GPSFTIGKAIWLLWGLVFNNSVPVQNPKGTTSKIM VSVWAFFAVIFLASYTANLAAFMIQEEFVDQVTGL SDKKFQRPHDYSPPFRFGTVPNGSTERNIRNNYPY MHQYMTKFNQKGVEDALVSLKTGKLDAFIYDAAVL NYKAGRDEGCKLVTIGSGYIFATTGYGIALQKGSP WKRQIDLALLQFVGDGEMEELETLWLTGICHNEKN EVMSSQLDIDNMAGVFYMLAAAMALSLITFIWEHL FYWKLRFCFTGVCSDRPGLLFSISRGIYSCIHGVH IEEKKKSPDFNLTGSQSNMLKLLRSAKNISSMSNM NSSRMDSPKRAADFIQRGSLIMDMVSDKGNLMYSD NRSFQGKESIFGDNMNELQTFVANRQKDNLNNYVF QGQHPLTLNESNPNTVEVAVSTESKANSRPRQLWK KSVDSIRQDSLSQNPVSQRDEATAENRTHSLKSPR YLPEEMAHSDISETSNRATCHREPDNSKNHKTKDN FKRSVASKYPKDCSEVERTYLKTKSSSPRDKIYTI DGEKEPGFHLDPPQFVENVTLPENVDFPDPYQDPS ENFRKGDSTLPMNRNPLHNEEGLSNNDQYKLYSKH FTLKDKGSPHSETSERYRQNSTHCRSCLSNMPTYS GHFTMRSPFKCDACLRMGNLYDIDEDQMLQETGNP ATGEQVYQQDWAQNNALQLQKNKLRISRQHSYDNI VDKPRELDLSRPSRSISLKDRERLLEGNFYGSLFS VPSSKLSGKKSSLFPQGLEDSKRSKSLLPDHTSDN PFLHSHRDDQRLVIGRCPSDPYKHSLPSQAVNDSY LRSSLRSTASYCSRDSRGHNDVYISEHVMPYAANK NNMYSTPRVLNSCSNRRVYKKMPSIESDV
Sodium- and chloride-dependent GABA transporter 1 (SLC6A1)	SLC6A1-Related Disorder; Myoclonic-atonic epilepsy	237	MATNGSKVADGQISTEVSEAPVANDKPKTLVVKVQ KKAADLPDRDTWKGRFDFLMSCVGYAIGLGNVWRF PYLCGKNGGGAFLIPYFLTLIFAGVPLFLLECSLG QYTSIGGLGVWKLAPMFKGVGLAAAVLSFWLNIYY IVIISWAIYYLYNSFTTTLPWKQCDNPWNTDRCFS NYSMVNTTNMTSAVVEFWERNMHQMTDGLDKPGQI RWPLAITLAIAWILVYFCIWKGVGWTGKVVYFSAT YPYIMLIILFFRGVTLPGAKEGILFYITPNFRKLS DSEVWLDAATQIFFSYGLGLGSLIALGSYNSFHNN VYRDSIIVCCINSCTSMFAGFVIFSIVGFMAHVTK RSIADVAASGPGLAFLAYPEAVTQLPISPLWAILF FSMLLMLGIDSQFCTVEGFITALVDEYPRLLRNRR ELFIAAVCIISYLIGLSNITQGGIYVFKLFDYYSA SGMSLLFLVFFECVSISWFYGVNRFYDNIQEMVGS RPCIWWKLCWSFFTPIIVAGVFIFSAVQMTPLTMG NYVFPKWGQGVGWLMALSSMVLIPGYMAYMFLTLK GSLKQRIQVMVQPSEDIVRPENGPEQPQAGSSTSK EAYI
Sodium/potassium-transporting ATPase subunit alpha-2	Alternating hemiplegia of childhood	238	MGRGAGREYSPAATTAENGGGKKKQKEKELDELKK EVAMDDHKLSLDELGRKYQVDLSKGLTNQRAQDVL ARDGPNALTPPPTTPEWVKFCRQLFGGFSILLWIG AILCFLAYGIQAAMEDEPSNDNLYLGVVLAAVVIV TGCFSYYQEAKSSKIMDSFKNMVPQQALVIREGEK

(ATP1A2) Signal Sequence Underlined			MQINAEEVVVGDLVEVKGGDRVPADLRIISSHGCK VDNSSLTGESEPQTRSPEFTHENPLETRNICFFST NCVEGTARGIVIATGDRTVMGRIATLASGLEVGRT PIAMEIEHFIQLITGVAVFLGVSFFVLSLILGYSW LEAVIFLIGIIVANVPEGLLATVTVCLTLTAKRMA RKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMT VAHMWFDNQIHEADTTEDQSGATFDKRSPTWTALS RIAGLCNRAVFKAGQENISVSKRDTAGDASESALL KCIELSCGSVRKMRDRNPKVAEIPFNSTNKYQLSI HEREDSPQSHVLVMKGAPERILDRCSTILVQGKEI PLDKEMQDAFQNAYMELGGLGERVLGFCQLNLPSG KFPRGFKFDTDELNFPTEKLCFVGLMSMIDPPRAA VPDAVGKCRSAGIKVIMVTGDHPITAKAIAKGVGI ISEGNETVEDIAARLNIPMSQVNPREAKACVVHGS DLKDMTSEQLDEILKNHTEIVFARTSPQQKLIIVE GCQRQGAIVAVTGDGVNDSPALKKADIGIAMGISG SDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLK KSIAYTLTSNIPEITPFLLFIIANIPLPLGTVTIL CIDLGTDMVPAISLAYEAAESDIMKRQPRNSQTDK LVNERLISMAYGQIGMIQALGGFFTYFVILAENGF LPSRLLGIRLDWDDRTMNDLEDSYGQEWTYEQRKV VEFTCHTAFFASIVVVQWADLIICKTRRNSVFQQG MKNKILIFGLLEETALAAFLSYCPGMGVALRMYPL KVTWWFCAFPYSLLIFIYDEVRKLILRRYPGGWVE KETYY
Sodium/potassium-transporting ATPase subunit alpha-3 (ATP1A3)	Alternating hemiplegia of childhood 2	239	MGDKKDDKDSPKKNKGKERRDLDDLKKEVAMTEHK MSVEEVCRKYNTDCVQGLTHSKAQEILARDGPNAL TPPPTTPEWVKFCRQLFGGFSILLWIGAILCFLAY GIQAGTEDDPSGDNLYLGIVLAAVVIITGCFSYYQ EAKSSKIMESFKNMVPQQALVIREGEKMQVNAEEV VVGDLVEIKGGDRVPADLRIISAHGCKVDNSSLTG ESEPQTRSPDCTHDNPLETRNITFFSTNCVEGTAR GVVVATGDRTVMGRIATLASGLEVGKTPIAIEIEH FIQLITGVAVFLGVSFFILSLILGYTWLEAVIFLI GIIVANVPEGLLATVTVCLTLTAKRMARKNCLVKN LEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDN QIHEADTTEDQSGTSFDKSSHTWVALSHIAGLCNR AVFKGGQDNIPVLKRDVAGDASESALLKCIELSSG SVKLMRERNKKVAEIPFNSTNKYQLSIHETEDPND NRYLLVMKGAPERILDRCSTILLQGKEQPLDEEMK EAFQNAYLELGGLGERVLGFCHYYLPEEQFPKGFA FDCDDVNFTTDNLCFVGLMSMIDPPRAAVPDAVGK CRSAGIKVIMVTGDHPITAKAIAKGVGIISEGNET VEDIAARLNIPVSQVNPRDAKACVIHGTDLKDFTS EQIDEILQNHTEIVFARTSPQQKLIIVEGCQRQGA IVAVTGDGVNDSPALKKADIGVAMGIAGSDVSKQA ADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTL TSNIPEITPFLLFIMANIPLPLGTITILCIDLGTD MVPAISLAYEAAESDIMKRQPRNPRTDKLVNERLI SMAYGQIGMIQALGGFFSYFVILAENGFLPGNLVG IRLNWDDRTVNDLEDSYGQQWTYEQRKVVEFTCHT

			AFFVSIVVVQWADLIICKTRRNSVFQQGMKNKILI FGLFEETALAAFLSYCPGMDVALRMYPLKPSWWFC AFPYSFLIFVYDEIRKLILRRNPGGWVEKETYY
Sodium channel protein type 9 subunit alpha (SCN9A)	SCN9A Epilepsy; Epilepsy, generalized, with febrile seizures plus, type 7	240	MAMLPPPGPQSFVHFTKQSLALIEQRIAERKSKEP KEEKKDDDEEAPKPSSDLEAGKQLPFIYGDIPPGM VSEPLEDLDPYYADKKTFIVLNKGKTIFRFNATPA LYMLSPFSPLRRISIKILVHSLFSMLIMCTILTNC IFMTMNNPPDWTKNVEYTFTGIYTFESLVKILARG FCVGEFTFLRDPWNWLDFVVIVFAYLTEFVNLGNV SALRTFRVLRALKTISVIPGLKTIVGALIQSVKKL SDVMILTVFCLSVFALIGLQLFMGNLKHKCFRNSL ENNETLESIMNTLESEEDFRKYFYYLEGSKDALLC GFSTDSGQCPEGYTCVKIGRNPDYGYTSFDTFSWA FLALFRLMTQDYWENLYQQTLRAAGKTYMIFFVVV IFLGSFYLINLILAVVAMAYEEQNQANIEEAKQKE LEFQQMLDRLKKEQEEAEAIAAAAAEYTSIRRSRI MGLSESSSETSKLSSKSAKERRNRRKKKNQKKLSS GEEKGDAEKLSKSESEDSIRRKSFHLGVEGHRRAH EKRLSTPNQSPLSIRGSLFSARRSSRTSLFSFKGR GRDIGSETEFADDEHSIFGDNESRRGSLFVPHRPQ ERRSSNISQASRSPPMLPVNGKMHSAVDCNGVVSL VDGRSALMLPNGQLLPEVIIDKATSDDSGTTNQIH KKRRCSSYLLSEDMLNDPNLRQRAMSRASILTNTV EELEESRQKCPPWWYRFAHKFLIWNCSPYWIKFKK CIYFIVMDPFVDLAITICIVLNTLFMAMEHHPMTE EFKNVLAIGNLVFTGIFAAEMVLKLIAMDPYEYFQ VGWNIFDSLIVTLSLVELFLADVEGLSVLRSFRLL RVFKLAKSWPTLNMLIKIIGNSVGALGNLTLVLAI IVFIFAVVGMQLFGKSYKECVCKINDDCTLPRWHM NDFFHSFLIVFRVLCGEWIETMWDCMEVAGQAMCL IVYMMVMVIGNLVVLNLFLALLLSSFSSDNLTAIE EDPDANNLQIAVTRIKKGINYVKQTLREFILKAFS KKPKISREIRQAEDLNTKKENYISNHTLAEMSKGH NFLKEKDKISGFGSSVDKHLMEDSDGQSFIHNPSL TVTVPIAPGESDLENMNAEELSSDSDSEYSKVRLN RSSSSECSTVDNPLPGEGEEAEAEPMNSDEPEACF TDGCVWRFSCCQVNIESGKGKIWWNIRKTCYKIVE HSWFESFIVLMILLSSGALAFEDIYIERKKTIKII LEYADKIFTYIFILEMLLKWIAYGYKTYFTNAWCW LDFLIVDVSLVTLVANTLGYSDLGPIKSLRTLRAL RPLRALSRFEGMRVVVNALIGAIPSIMNVLLVCLI FWLIFSIMGVNLFAGKFYECINTTDGSRFPASQVP NRSECFALMNVSQNVRWKNLKVNFDNVGLGYLSLL QVATFKGWTIIMYAAVDSVNVDKQPKYEYSLYMYI YFVVFIIFGSFFTLNLFIGVIIDNFNQQKKKLGGQ DIFMTEEQKKYYNAMKKLGSKKPQKPIPRPGNKIQ GCIFDLVTNQAFDISIMVLICLNMVTMMVEKEGQS QHMTEVLYWINVVFIILFTGECVLKLISLRHYYFT VGWNIFDFVVVIISIVGMFLADLIETYFVSPTLFR VIRLARIGRILRLVKGAKGIRTLLFALMMSLPALF NIGLLLFLVMFIYAIFGMSNFAYVKKEDGINDMFN

			FETFGNSMICLFQITTSAGWDGLLAPILNSKPPDC DPKKVHPGSSVEGDCGNPSVGIFYFVSYIIISFLV VVNMYIAVILENFSVATEESTEPLSEDDFEMFYEV WEKFDPDATQFIEFSKLSDFAAALDPPLLIAKPNK VQLIAMDLPMVSGDRIHCLDILFAFTKRVLGESGE MDSLRSQMEERFMSANPSKVSYEPITTTLKRKQED VSATVIQRAYRRYRLRQNVKNISSIYIKDGDRDDD LLNKKDMAFDNVNENSSPEKTDATSSTTSPPSYDS VTKPDKEKYEQDRTEKEDKGKDSKESKK
Gamma-aminobutyric acid receptor subunit beta-3 (GABRB3) Signal Sequence Underlined	GABRB3 Associated Epilepsy	241	MWGLAGGRLFGIFSAPVLVAVVCCAQSVNDPGNMS FVKETVDKLLKGYDIRLRPDFGGPPVCVGMNIDIA SIDMVSEVNMDYTLTMYFQQYWRDKRLAYSGIPLN LTLDNRVADQLWVPDTYFLNDKKSFVHGVTVKNRM IRLHPDGTVLYGLRITTTAACMMDLRRYPLDEQNC TLEIESYGYTTDDIEFYWRGGDKAVTGVERIELPQ FSIVEHRLVSRNVVFATGAYPRLSLSFRLKRNIGY FILQTYMPSILITILSWVSFWINYDASAARVALGI TTVLTMTTINTHLRETLPKIPYVKAIDMYLMGCFV FVFLALLEYAFVNYIFFGRGPQRQKKLAEKTAKAK NDRSKSESNRVDAHGNILLTSLEVHNEMNEVSGGI GDTRNSAISFDNSGIQYRKQSMPREGHGRFLGDRS LPHKKTHLRRRSSQLKIKIPDLTDVNAIDRWSRIV FPFTFSLFNLVYWLYYVN
Potassium voltage-gated channel subfamily KQT member 3 (KCNQ3)	Heterotetramerizes with KCNQ2 KCNQ2-Related Disorders (Epileptic Encephalopathy)	242	MGLKARRAAGAAGGGGDGGGGGGGAANPAGGDAAA AGDEERKVGLAPGDVEQVTLALGAGADKDGTLLLE GGGRDEGQRRTPQGIGLLAKTPLSRPVKRNNAKYR RIQTLIYDALERPRGWALLYHALVFLIVLGCLILA VLTTFKEYETVSGDWLLLLETFAIFIFGAEFALRI WAAGCCCRYKGWRGRLKFARKPLCMLDIFVLIASV PVVAVGNQGNVLATSLRSLRFLQILRMLRMDRRGG TWKLLGSAICAHSKELITAWYIGFLTLILSSFLVY LVEKDVPEVDAQGEEMKEEFETYADALWWGLITLA TIGYGDKTPKTWEGRLIAATFSLIGVSFFALPAGI LGSGLALKVQEQHRQKHFEKRRKPAAELIQAAWRY YATNPNRIDLVATWRFYESVVSFPFFRKEQLEAAS SQKLGLLDRVRLSNPRGSNTKGKLFTPLNVDAIEE SPSKEPKPVGLNNKERFRTAFRMKAYAFWQSSEDA GTGDPMAEDRGYGNDFPIEDMIPTLKAAIRAVRIL QFRLYKKKFKETLRPYDVKDVIEQYSAGHLDMLSR IKYLQTRIDMIFTPGPPSTPKHKKSQKGSAFTFPS QQSPRNEPYVARPSTSEIEDQSMMGKFVKVERQVQ DMGKKLDFLVDMHMQHMERLQVQVTEYYPTKGTSS PAEAEKKEDNRYSDLKTIICNYSETGPPEPPYSFH QVTIDKVSPYGFFAHDPVNLPRGGPSSGKVQATPP SSATTYVERPTVLPILTLLDSRVSCHSQADLQGPY SDRISPRQRRSITRDSDTPLSLMSVNHEELERSPS GFSISQDRDDYVFGPNGGSSWMREKRYLAEGETDT DTDPFTPSGSMPLSSTGDGISDSVWTPSNKPI
Rhodopsin (RHO)	Autosomal Dominant RP	243	MNGTEGPNFYVPFSNATGVVRSPFEYPQYYLAEPW QFSMLAAYMFLLIVLGFPINFLTLYVTVQHKKLRT PLNYILLNLAVADLFMVLGGFTSTLYTSLHGYFVF

			GPTGCNLEGFFATLGGEIALWSLVVLAIERYVVVC KPMSNFRFGENHAIMGVAFTWVMALACAAPPLAGW SRYIPEGLQCSCGIDYYTLKPEVNNESFVIYMFVV HFTIPMIIIFFCYGQLVFTVKEAAAQQQESATTQK AEKEVTRMVIIMVIAFLICWVPYASVAFYIFTHQG SNFGPIFMTIPAFFAKSAAIYNPVIYIMMNKQFRN CMLTTICCGKNPLGDDEASATVSKTETSQVAPA
Protein jagged-1 (JAG1) Signal Peptide Underlined	Alagille syndrome 1	244	MRSPRTRGRSGRPLSLLLALLCALRAKVCGASGQF ELEILSMQNVNGELQNGNCCGGARNPGDRKCTRDE CDTYFKVCLKEYQSRVTAGGPCSFGSGSTPVIGGN TFNLKASRGNDRNRIVLPFSFAWPRSYTLLVEAWD SSNDTVQPDSIIEKASHSGMINPSRQWQTLKQNTG VAHFEYQIRVTCDDYYYGFGCNKFCRPRDDFFGHY ACDQNGNKTCMEGWMGPECNRAICRQGCSPKHGSC KLPGDCRCQYGWQGLYCDKCIPHPGCVHGICNEPW QCLCETNWGGQLCDKDLNYCGTHQPCLNGGTCSNT GPDKYQCSCPEGYSGPNCEIAEHACLSDPCHNRGS CKETSLGFECECSPGWTGPTCSTNIDDCSPNNCSH GGTCQDLVNGFKCVCPPQWTGKTCQLDANECEAKP CVNAKSCKNLIASYYCDCLPGWMGQNCDININDCL GQCQNDASCRDLVNGYRCICPPGYAGDHCERDIDE CASNPCLNGGHCQNEINRFQCLCPTGFSGNLCQLD IDYCEPNPCQNGAQCYNRASDYFCKCPEDYEGKNC SHLKDHCRTTPCEVIDSCTVAMASNDTPEGVRYIS SNVCGPHGKCKSQSGGKFTCDCNKGFTGTYCHENI NDCESNPCRNGGTCIDGVNSYKCICSDGWEGAYCE TNINDCSQNPCHNGGTCRDLVNDFYCDCKNGWKGK TCHSRDSQCDEATCNNGGTCYDEGDAFKCMCPGGW EGTTCNIARNSSCLPNPCHNGGTCVVNGESFTCVC KEGWEGPICAQNTNDCSPHPCYNSGTCVDGDNWYR CECAPGFAGPDCRININECQSSPCAFGATCVDEIN GYRCVCPPGHSGAKCQEVSGRPCITMGSVIPDGAK WDDDCNTCQCLNGRIACSKVWCGPRPCLLHKGHSE CPSGQSCIPILDDQCFVHPCTGVGECRSSSLQPVK TKCTSDSYYQDNCANITFTFNKEMMSPGLTTEHIC SELRNLNILKNVSAEYSIYIACEPSPSANNEIHVA ISAEDIRDDGNPIKEITDKIIDLVSKRDGNSSLIA AVAEVRVQRRPLKNRTDFLVPLLSSVLTVAWICCL VTAFYWCLRKRRKPGSHTHSASEDNTTNNVREQLN QIKNPIEKHGANTVPIKDYENKNSKMSKIRTHNSE VEEDDMDKHQQKARFAKQPAYTLVDREEKPPNGTP TKHPNWTNKQDNRDLESAQSLNRMEYIV
Inositol 1,4,5-trisphosphate receptor type 1 (ITPR1)	Gillespie Syndrome	245	MSDKMSSFLHIGDICSLYAEGSTNGFISTLGLVDD RCVVQPETGDLNNPPKKFRDCLFKLCPMNRYSAQK QFWKAAKPGANSTTDAVLLNKLHHAADLEKKQNET ENRKLLGTVIQYGNVIQLLHLKSNKYLTVNKRLPA LLEKNAMRVTLDEAGNEGSWFYIQPFYKLRSIGDS VVIGDKVVLNPVNAGQPLHASSHQLVDNPGCNEVN SVNCNTSWKIVLFMKWSDNKDDILKGGDVVRLFHA EQEKFLTCDEHRKKQHVFLRTTGRQSATSATSSKA LWEVEVVQHDPCRGGAGYWNSLFRFKHLATGHYLA

			AEVDPDFEEECLEFQPSVDPDQDASRSRLRNAQEK MVYSLVSVPEGNDISSIFELDPTTLRGGDSLVPRN SYVRLRHLCTNTWVHSTNIPIDKEEEKPVMLKIGT SPVKEDKEAFAIVPVSPAEVRDLDFANDASKVLGS IAGKLEKGTITQNERRSVTKLLEDLVYFVTGGTNS GQDVLEVVFSKPNRERQKLMREQNILKQIFKLLQA PFTDCGDGPMLRLEELGDQRHAPFRHICRLCYRVL RHSQQDYRKNQEYIAKQFGFMQKQIGYDVLAEDTI TALLHNNRKLLEKHITAAEIDTFVSLVRKNREPRF LDYLSDLCVSMNKSIPVTQELICKAVLNPTNADIL IETKLVLSRFEFEGVSSTGENALEAGEDEEEVWLF WRDSNKEIRSKSVRELAQDAKEGQKEDRDVLSYYR YQLNLFARMCLDRQYLAINEISGQLDVDLILRCMS DENLPYDLRASFCRLMLHMHVDRDPQEQVTPVKYA RLWSEIPSEIAIDDYDSSGASKDEIKERFAQTMEF VEEYLRDVVCQRFPFSDKEKNKLTFEVVNLARNLI YFGFYNFSDLLRLTKILLAILDCVHVTTIFPISKM AKGEENKGNNDVEKLKSSNVMRSIHGVGELMTQVV LRGGGFLPMTPMAAAPEGNVKQAEPEKEDIMVMDT KLKIIEILQFILNVRLDYRISCLLCIFKREFDESN SQTSETSSGNSSQEGPSNVPGALDFEHIEEQAEGI FGGSEENTPLDLDDHGGRTFLRVLLHLTMHDYPPL VSGALQLLFRHFSQRQEVLQAFKQVQLLVTSQDVD NYKQIKQDLDQLRSIVEKSELWVYKGQGPDETMDG ASGENEHKKTEEGNNKPQKHESTSSYNYRVVKEIL IRLSKLCVQESASVRKSRKQQQRLLRNMGAHAVVL ELLQIPYEKAEDTKMQEIMRLAHEFLQNFCAGNQQ NQALLHKHINLFLNPGILEAVTMQHIFMNNFQLCS EINERVVQHFVHCIETHGRNVQYIKFLQTIVKAEG KFIKKCQDMVMAELVNSGEDVLVFYNDRASFQTLI QMMRSERDRMDENSPLMYHIHLVELLAVCTEGKNV YTEIKCNSLLPLDDIVRVVTHEDCIPEVKIAYINF LNHCYVDTEVEMKEIYTSNHMWKLFENFLVDICRA CNNTSDRKHADSILEKYVTEIVMSIVTTFFSSPFS DQSTTLQTRQPVFVQLLQGVFRVYHCNWLMPSQKA SVESCIRVLSDVAKSRAIAIPVDLDSQVNNLFLKS HSIVQKTAMNWRLSARNAARRDSVLAASRDYRNII ERLQDIVSALEDRLRPLVQAELSVLVDVLHRPELL FPENTDARRKCESGGFICKLIKHTKQLLEENEEKL CIKVLQTLREMMTKDRGYGEKLISIDELDNAELPP APDSENATEELEPSPPLRQLEDHKRGEALRQVLVN RYYGNVRPSGRRESLTSFGNGPLSAGGPGKPGGGG GGSGSSSMSRGEMSLAEVQCHLDKEGASNLVIDLI MNASSDRVFHESILLAIALLEGGNTTIQHSFFCRL TEDKKSEKFFKVFYDRMKVAQQEIKATVTVNTSDL GNKKKDDEVDRDAPSRKKAKEPTTQITEEVRDQLL EASAATRKAFTTFRREADPDDHYQPGEGTQATADK AKDDLEMSAVITIMQPILRFLQLLCENHNRDLQNF LRCQNNKTNYNLVCETLQFLDCICGSTTGGLGLLG LYINEKNVALINQTLESLTEYCQGPCHENQNCIAT HESNGIDIITALILNDINPLGKKRMDLVLELKNNA

			SKLLLAIMESRHDSENAERILYNMRPKELVEVIKK AYMQGEVEFEDGENGEDGAASPRNVGHNIYILAHQ LARHNKELQSMLKPGGQVDGDEALEFYAKHTAQIE IVRLDRTMEQIVFPVPSICEFLTKESKLRIYYTTE RDEQGSKINDFFLRSEDLFNEMNWQKKLRAQPVLY WCARNMSFWSSISFNLAVLMNLLVAFFYPFKGVRG GTLEPHWSGLLWTAMLISLAIVIALPKPHGIRALI ASTILRLIFSVGLQPTLFLLGAFNVCNKIIFLMSF VGNCGTFTRGYRAMVLDVEFLYHLLYLVICAMGLF VHEFFYSLLLFDLVYREETLLNVIKSVTRNGRSII LTAVLALILVYLFSIVGYLFFKDDFILEVDRLPNE TAVPETGESLASEFLFSDVCRVESGENCSSPAPRE ELVPAEETEQDKEHTCETLLMCIVTVLSHGLRSGG GVGDVLRKPSKEEPLFAARVIYDLLFFFMVIIIVL NLIFGVIIDTFADLRSEKQKKEEILKTTCFICGLE RDKFDNKTVTFEEHIKEEHNMWHYLCFIVLVKVKD STEYTGPESYVAEMIKERNLDWFPRMRAMSLVSSD SEGEQNELRNLQEKLESTMKLVTNLSGQLSELKDQ MTEQRKQKQRIGLLGHPPHMNVNPQQPA
Sugar transporter SWEET1 (SLC50A1)	-	294	MEAGGFLDSLIYGACVVFTLGMFSAGLSDLRHMRM TRSVDNVQFLPFLTTEVNNLGWLSYGALKGDGILI VVNTVGAALQTLYILAYLHYCPRKRVVLLQTATLL GVLLLGYGYFWLLVPNPEARLQQLGLFCSVFTISM YLSPLADLAKVIQTKSTQCLSYPLTIATLLTSASW CLYGFRLRDPYIMVSNFPGIVTSFIRFWLFWKYPQ EQDRNYWLLQT
Transmembrane protein 258 (TMEM258)	-	295	MELEAMSRYTSPVNPAVFPHLTVVLLAIGMFFTAW FFVYEVTSTKYTRDIYKELLISLVASLFMGFGVLF LLLWVGIYV
Follicle-stimulating hormone receptor (FSHR) Signal Sequence Underlined	Ovarian dysgenesis 1 (ODG1)	296	MALLLVSLLAFLSLGSGCHHRICHCSNRVFLCQES KVTEIPSDLPRNAIELRFVLTKLRVIQKGAFSGFG DLEKIEISQNDVLEVIEADVFSNLPKLHEIRIEKA NNLLYINPEAFQNLPNLQYLLISNTGIKHLPDVHK IHSLQKVLLDIQDNINIHTIERNSFVGLSFESVIL WLNKNGIQEIHNCAFNGTQLDELNLSDNNNLEELP NDVFHGASGPVILDISRTRIHSLPSYGLENLKKLR ARSTYNLKKLPTLEKLVALMEASLTYPSHCCAFAN WRRQISELHPICNKSILRQEVDYMTQARGQRSSLA EDNESSYSRGFDMTYTEFDYDLCNEVVDVTCSPKP DAFNPCEDIMGYNILRVLIWFISILAITGNIIVLV ILTTSQYKLTVPRFLMCNLAFADLCIGIYLLLIAS VDIHTKSQYHNYAIDWQTGAGCDAAGFFTVFASEL SVYTLTAITLERWHTITHAMQLDCKVQLRHAASVM VMGWIFAFAAALFPIFGISSYMKVSICLPMDIDSP LSQLYVMSLLVLNVLAFVVICGCYIHIYLTVRNPN IVSSSSDTRIAKRMAMLIFTDFLCMAPISFFAISA SLKVPLITVSKAKILLVLFHPINSCANPFLYAIFT KNFRRDFFILLSKCGCYEMQAQIYRTETSSTVHNT HPRNGHCSSAPRVTNGSTYILVPLSHLAQN

5.3.3 Orientation and Linkers

[00219] In some embodiments, the effector domain is N-terminal of the targeting domain in the fusion protein. In some embodiments, the targeting domain is N-terminal of the effector domain in the fusion protein. In some embodiments, the effector domain is operably connected (directly or indirectly) to the C terminus of the targeting domain. In some embodiments, the effector domain is operably connected (directly or indirectly) to the N terminus of the targeting domain. In some embodiments, the effector domain is directly operably connected to the C terminus of the targeting domain. In some embodiments, the effector domain is directly operably connected to the N terminus of the targeting domain.

[00220] In some embodiments, the effector domain is indirectly operably connected to the C terminus of the targeting domain. In some embodiments, the effector domain is indirectly operably connected to the N terminus of the targeting domain. One or more amino acid sequences comprising e.g., a linker, or encoding one or more polypeptides may be positioned between the effector moiety and the targeting moiety. In some embodiments, the effector domain is indirectly operably connected to the C terminus of the targeting domain through a peptide linker. In some embodiments, the effector domain is indirectly operably connected to the N terminus of the targeting domain through a peptide linker.

[00221] Each component of the fusion protein described herein can be directly linked to the other to indirectly linked to the other via a peptide linker. [0080] Any suitable peptide linker known in the art can be used that enables the effector domain and the targeting domain to bind their respective antigens. In some embodiments, the linker is one or any combination of a cleavable linker, a non-cleavable linker, a peptide linker, a flexible linker, a rigid linker, a helical linker, or a non-helical linker. In some embodiments, the linker is a peptide linker. In some embodiments, the linker is a peptide linker that comprises glycine or serine, or both glycine and serine amino acid residues. In some embodiments, the peptide linker comprises from about 1-20, 1-15, 1-10, 1-5, 5-20, 5-15, 5-10, or 15-20 amino acids. In some embodiments, the peptide linker comprises from or from about 2-25, 5-25, 10-25, 15-25, 20-25, 2-20, 5-20, 10-20, 15-20, 2-15, 5-15, 10-15, 2-10, or 5-10 amino acids. In some embodiments, the linker is a peptide linker that consists of glycine or serine, or both glycine and serine amino acid residues. In some embodiments, the

peptide linker consists of from or from about 2-25, 5-25, 10-25, 15-25, 20-25, 2-20, 5-20, 10-20, 15-20, 2-15, 5-15, 10-15, 2-10, or 5-10 amino acids. In some embodiments, the peptide linker comprises at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 amino acid residues. In some embodiments, the linker is at least 11 amino acids in length. In some embodiments, the linker is at least 15 amino acids in length. In some embodiments, the linker is 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 amino acid residues in length.

[00222] In some embodiments, the linker is a glycine/serine linker, e.g., a peptide linker substantially consisting of the amino acids glycine and serine. In some embodiments, the linker is a glycine/serine/proline linker, e.g., a peptide linker substantially consisting of the amino acids glycine, serine, and proline.

[00223] In some embodiments, the amino acid sequence of the linker comprises the amino acid sequence of any one of SEQ ID NOS: 297-424, or the amino acid sequence of any one of SEQ ID NOS: 297-424 comprising 1, 2, or 3 amino acid modifications (e.g., a substitution, deletion, or addition). In some embodiments, the amino acid sequence of the linker consists of the amino acid sequence of any one of SEQ ID NOS: 297-424, or the amino acid sequence of any one of SEQ ID NOS: 297-424 comprising 1, 2, or 3 amino acid modifications (e.g., a substitution, deletion, or addition).

[00224] In some embodiments, the amino acid sequence of the linker comprises the amino acid sequence of any one of SEQ ID NOS: 297-306, or the amino acid sequence of any one of SEQ ID NOS: 297-288 comprising 1, 2, or 3 amino acid modifications (e.g., a substitution, deletion, or addition). In some embodiments, the amino acid sequence of the linker consists of the amino acid sequence of any one of SEQ ID NOS: 297-306, or the amino acid sequence of any one of SEQ ID NOS: 297-306 comprising 1, 2, or 3 amino acid modifications (e.g., a substitution, deletion, or addition).

[00225] The amino acid sequence of exemplary linkers for use in any one or more of the fusion proteins described herein is provided in Table 3 below.

Table 3. Amino Acid Sequence of Exemplary Linkers

Amino Acid Sequence	SEQ ID NO
GGGGSGGGGSGGGGSGGGGSGGGGS	297
GGGGSGGGGSGGGGSGGGGS	298
GGGGSGGGGSGGGGS	299
GGGGSGGGGS	300

GGGGS	301
SGGGGSGGGGSGGGGS	302
SGGGGSGGGGSGGGG	303
SGGGGSGGGG	304
SGGGG	305
GGSGG	306
AHFKISGEKRPSTDPGKKAKNPKKKKKKDP	307
AHRAKKMSKTHA	308
ASPEYVNLPINGNG	309
CTKRPRW	310
DKAKRVSRNKSEKKRR	311
EELRLKEELLKGIYA	312
EEQLRRRKNSRLNNTG	313
EVLKVIRTGKRKKKAWKRMVTKVC	314
HHHHHHHHHHHHQPH	315
HKKKHPDASVNFSEFSK	316
HKRTKKNLS	317
IINGRKLKLKKSRRRSSQTSNNSFTSRRS	318
KAEQERRK	319
KEKRKRREELFIEQKKRK	320
KKGKDEWFSRGKKP	321
KKGPSVQKRKKTNLS	322
KKKTVINDLLHYKKEK	323
KKNGGKGKNKPSAKIKK	324
KKPKWDDFKKKKK	325
KKRKKDNLS	326
KKRRKRRRK	327
KKRRRRARK	328
KKSKRGR	329
KKSRKRGS	330
KKSTALSRELGKIMRRR	331
KKSYQDPEIIAHSRPRK	332
KKTGKNRKLKSKRVKTR	333
KKVSIAGQSGKLWRWKR	334
KKYENVVIKRSPRKRGRPRK	335
KNKKRK	336
KPKKKR	337
KRAMKDDSHGNSTSPKRRK	338
KRANSNLVAAYEKAKKK	339
KRASEDTTSGSPPKKSSAGPKR	340
KRFKRRWMVRKMKTKK	341
KRGLNSSFETSPKKVK	342
KRGNSSIGPNDLSKRKQRKK	343
KRIHSVSLSQSQIDPSKKVKRAK	344
KRKGKLKNKGSKRKK	345
KRRRRRRREKRKR	346
KRSNDRTYSPEEEKQRRA	347
KRTVATNGDASGAHRAKKMSK	348
KRVYNKGEDEQEHLPKGKKR	349

KSGKAPRRRAVSMDNSNK	350
KVNFLDMSLDDIIIYKELE	351
KVQHRIAKKTTRRRR	352
LSPSLSPL	353
MDSLLMNRRKFLYQFKNVRWAKGRRETYLC	354
MPQNEYIELHRKRYGYRLDYHEKKRKKESREAHERSKKAKKMIGLKAKLYHK	355
MVQLRPRASR	356
NNKLLAKRRKGGASPKDDPMDDIK	357
NYKRPMDGTYGPPAKRHEGE	358
PDTKRAKLDSSETTMVKKK	359
PEKRTKI	360
PGGRGKKK	361
PGKMDKGEHRQERRDRPY	362
PKKGDKYDKTD	363
PKKKSRK	364
PKKNKPE	365
PKKRAKV	366
PKPKKLKVE	367
PKRGRGR	368
PKRRLVDDA	369
PKRRRTY	370
PLFKRR	371
PLRKAKR	372
PPAKRKCIF	373
PPARRRRL	374
PPKKKRKV	375
PPNKRMKVKH	376
PPRIYPQLPSAPT	377
PQRSPFPKSSVKR	378
PRPRKVPR	379
PRRRVQRKR	380
PRRVRLK	381
PSRKRPR	382
PSSKKRKV	383
PTKKRVK	384
QRPGPYDRP	385
RGKGGKGLGKGGAKRHRK	386
RKAGKGGGGHKTTKKRSAKDEKVP	387
RKIKLKRAK	388
RKIKRKRAK	389
RKKEAPGPREELRSRGR	390
RKKRKGK	391
RKKRRQRRR	392
RKKSIPLSIKNLKRKHKRKKNKITR	393
RKLVKPKNTKMKTKLRTNPY	394
RKRLILSDKGQLDWKK	395
RKRLKSK	396
RKRRVRDNM	397
RKRSPKDKKEKDLDGAGKRRKT	398

RKRTPRVDGQTGENDMNKRRRK	399
RLPVRRRRRR	400
RLRFRKPKSK	401
RQQRKR	402
RRDLNSSFETSPKKVK	403
RRDRAKLR	404
RRGDGRRR	405
RRGRKRKAEKQ	406
RRKKRR	407
RRKRSKSEDMDSVESKRRR	408
RRKRSR	409
RRPKGKTLQKRKPK	410
RRRGFERFGPDNMGRKRK	411
RRRGKNKVAAQNCRK	412
RRRKRRNLS	413
RRRQKQKGGASRRR	414
RRRREGPRARRRR	415
RRTIRLKLVYDKCDRSCKIQKKNRNKCQYCRFHKCLSVGMSHNAIRFGRMPRSEKAKL KAE	416
RRVPQRKEVSRCRKCRK	417
RVGGRRQAVECIEDLLNEPGQPLDLSCKRPRP	418
RVVKLRIAP	419
RVVRRR	420
SKRKTKISRKTR	421
SYVKTVPNRTRTYIKL	422
TGKNEAKKRKIA	423
TLSPASSPSSVSCPVIPASTDESPGSALNI	424

5.3.3.1 Conditional Constructs

[00226] Also described herein are constructs that comprise a targeting domain (e.g., a VHH, $(VHH)_2$) bound to an effector domain (e.g., an effector domain that comprises a catalytic domain of an deubiquitinase, or an effector domain that comprises a deubiquitinase). In some embodiments, the association of the targeting domain and the effector domain is mediated by binding of a first agent (e.g., a small molecule, protein, or peptide) attached to the targeting domain and a second agent (e.g., a small, molecule, protein, or peptide) attached to the effector domain. For example, in one embodiment, the targeting domain may be attached to a first agent that specifically binds to a second agent that is attached to the effector domain. In some embodiments, specific binding of the first agent to the second agent is mediated by addition of a third agent (e.g., a small molecule).

[00227] For example, a conditional construct includes an KBP/FRB-based dimerization switch, e.g., as described in US20170081411 (the entire contents of which are incorporated by reference

herein), can be utilized herein. FKBP12 (FKBP or FK506 binding protein) is an abundant cytoplasmic protein that serves as the initial intracellular target for the natural product immunosuppressive drug, rapamycin. Rapamycin binds to FKBP and to the large PI3K homolog FRAP (RAFT, mTOR), thereby acting to dimerize these molecules. In some embodiments, an FKBP/FRAP based switch, also referred to herein as an FKBP/FRB based switch, can utilize a heterodimerization molecule, e.g., rapamycin or a rapamycin analog. FRB is a 93 amino acid portion of FRAP, that is sufficient for binding the FKBP-rapamycin complex (Chen, J., Zheng, X. F., Brown, E. J. & Schreiber, S. L. (1995) Identification of an 11-kDa FKBP12-rapamycin-binding domain within the 289-kDa FKBP12-rapamycin-associated protein and characterization of a critical serine residue. Proc Natl Acad Sci USA 92: 4947-51), the entire contents of which is incorporated by reference herein. For example, the targeting domain can be attached to FKBP and the effector domain attached to FRB. Thereby, the association of the targeting domain and the effector domain is mediated by rapamycin and only takes place in the presence of rapamycin.

[00228] Exemplary conditional activation systems that can be used here include, but are not limited to those described in US20170081411; Lajoie MJ, et al. Designed protein logic to target cells with precise combinations of surface antigens. Science. 2020 Sep 25;369(6511):1637-1643. doi: 10.1126/science.aba6527. Epub 2020 Aug 20. PMID: 32820060; Farrants H, et al. Chemogenetic Control of Nanobodies. Nat Methods. 2020 Mar;17(3):279-282. doi: 10.1038/s41592-020-0746-7. Epub 2020 Feb 17. PMID: 32066961; and US20170081411, the entire contents of each of which is incorporated by reference herein for all purposes.

5.3.4 Exemplary Fusion Proteins

[00229] Exemplary fusion proteins of the present disclosure include, but are not limited to, those described below. In one embodiment, the fusion protein comprises an effector domain comprising a catalytic domain of a cysteine protease deubiquitinase, or a functional fragment or functional variant thereof; and a targeting domain comprising a targeting moiety that specifically binds a membrane protein, wherein the membrane protein is GRIN2B, CFTR, SCN1A, ATP7B, KCNQ2, SCN2A, CACNA1A, SLC2A1, SCN8A, PRRT2, GRIN2A, SLC6A1, USH2A, ATP1A2, ATP1A3, SCN9A, PCDH19, GABRB3, TSC2, TSC1, KCNQ3, DMD, RHO, JAG1, ITPR1, SLC50A1, TMEM258, or FSHR.

[00230] In one embodiment, the fusion protein comprises an effector domain comprising a

catalytic domain of a metalloprotease deubiquitinase, or a functional fragment or functional variant thereof; and a targeting domain comprising a targeting moiety that specifically binds a membrane protein, wherein the membrane protein is GRIN2B, CFTR, SCN1A, ATP7B, KCNQ2, SCN2A, CACNA1A, SLC2A1, SCN8A, PRRT2, GRIN2A, SLC6A1, USH2A, ATP1A2, ATP1A3, SCN9A, PCDH19, GABRB3, TSC2, TSC1, KCNQ3, DMD, RHO, JAG1, ITPR1, SLC50A1, TMEM258, or FSHR.

[00231] In one embodiment, the fusion protein comprises an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof, wherein the deubiquitinase is a ubiquitin-specific protease (USP), a ubiquitin C-terminal hydrolase (UCH), a Machado-Josephin domain protease (MJD), an ovarian tumour protease (OTU), a MINDY protease, or a ZUFSP protease; and a targeting domain comprising a targeting moiety that specifically binds a membrane protein, wherein the membrane protein is GRIN2B, CFTR, SCN1A, ATP7B, KCNQ2, SCN2A, CACNA1A, SLC2A1, SCN8A, PRRT2, GRIN2A, SLC6A1, USH2A, ATP1A2, ATP1A3, SCN9A, PCDH19, GABRB3, TSC2, TSC1, KCNQ3, DMD, RHO, JAG1, ITPR1, SLC50A1, TMEM258, or FSHR1.

[00232] In one embodiment, the fusion protein comprises an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof, wherein the deubiquitinase is selected from the group consisting of USP1, USP2, USP3, USP4, USP5, USP6, USP7, USP8, USP9X, USP9Y, USP10, USP11, USP12, USP13, USP14, USP15, USP16, USP17, USP17L2, USP17L3, USP17L4, USP17L5, USP17L7, USP17L8, USP18, USP19, USP20, USP21, USP22, USP23, USP24, USP25, USP26, USP27X, USP28, USP29, USP30, USP31, USP32, USP33, USP34, USP35, USP36, USP37, USP38, USP39, USP40, USP41, USP42, USP43, USP44, USP45, USP46, BAP1, UCHL1, UCHL3, UCHL5, ATXN3 ATXN3L, OTUB1, OTUB2 MINDY1, MINDY2, MINDY3, MINDY4, or ZUP1; and a targeting domain comprising a targeting moiety that specifically binds a membrane protein, wherein the membrane protein is GRIN2B, CFTR, SCN1A, ATP7B, KCNQ2, SCN2A, CACNA1A, SLC2A1, SCN8A, PRRT2, GRIN2A, SLC6A1, USH2A, ATP1A2, ATP1A3, SCN9A, PCDH19, GABRB3, TSC2, TSC1, KCNQ3, DMD, RHO, JAG1, ITPR1, SLC50A1, TMEM258, or FSHR.

[00233] In one embodiment, the fusion protein comprises an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof, wherein the deubiquitinase is described in Table 1; and a targeting domain comprising a targeting

moiety that specifically binds a membrane protein, wherein the membrane protein is GRIN2B, CFTR, SCN1A, ATP7B, KCNQ2, SCN2A, CACNA1A, SLC2A1, SCN8A, PRRT2, GRIN2A, SLC6A1, USH2A, ATP1A2, ATP1A3, SCN9A, PCDH19, GABRB3, TSC2, TSC1, KCNQ3, DMD, RHO, JAG1, ITPR1, SLC50A1, TMEM258, or FSHR.

[00234] In one embodiment, the fusion protein comprises an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof, wherein the catalytic domain is described in Table 1; and a targeting domain comprising a targeting moiety that specifically binds a membrane protein, wherein the membrane protein is GRIN2B, CFTR, SCN1A, ATP7B, KCNQ2, SCN2A, CACNA1A, SLC2A1, SCN8A, PRRT2, GRIN2A, SLC6A1, USH2A, ATP1A2, ATP1A3, SCN9A, PCDH19, GABRB3, TSC2, TSC1, KCNQ3, DMD, RHO, JAG1, ITPR1, SLC50A1, TMEM258, or FSHR.

[00235] In one embodiment, the fusion protein comprises an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof, wherein the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 1-112; and a targeting domain comprising a targeting moiety that specifically binds a membrane protein, wherein the membrane protein is GRIN2B, CFTR, SCN1A, ATP7B, KCNQ2, SCN2A, CACNA1A, SLC2A1, SCN8A, PRRT2, GRIN2A, SLC6A1, USH2A, ATP1A2, ATP1A3, SCN9A, PCDH19, GABRB3, TSC2, TSC1, KCNQ3, DMD, RHO, JAG1, ITPR1, SLC50A1, TMEM258, or FSHR.

[00236] In one embodiment, the fusion protein comprises an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof, wherein the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 113-220 or 293; and a targeting domain comprising a targeting moiety that specifically binds a membrane protein, wherein the membrane protein is GRIN2B, CFTR, SCN1A, ATP7B, KCNQ2, SCN2A, CACNA1A, SLC2A1, SCN8A, PRRT2, GRIN2A, SLC6A1, USH2A, ATP1A2, ATP1A3, SCN9A, PCDH19, GABRB3, TSC2, TSC1, KCNQ3, DMD, RHO, JAG1, ITPR1, SLC50A1, TMEM258, or FSHR.

[00237] In one embodiment, the fusion protein comprises an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof,

wherein the deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 1-112; and a targeting domain comprising a targeting moiety that specifically binds a membrane protein, wherein the membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 221-245 or 294-296.

[00238] In one embodiment, the fusion protein comprises an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof, wherein the catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 113-220 or 293; and a targeting domain comprising a targeting moiety that specifically binds a membrane protein, wherein the membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 221-245 or 294-296.

5.3.4.1 Additional Exemplary Embodiments

[00239] Additional exemplary embodiments of fusion proteins described herein are provided below, which should not be construed as limiting.

[00240] Embodiment 1. A fusion protein comprising: (a) an effector moiety comprising a functional fragment of a human deubiquitinase that is capable of mediating deubiquitination, wherein the human deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 1-112, and a targeting moiety comprising a VHH, $(VHH)_2$. or scFv that specifically binds to a membrane protein.

[00241] Embodiment 2. A fusion protein comprising an effector moiety comprising a functional fragment of a human deubiquitinase that is capable of mediating deubiquitination that comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 113-220 or 293, and a targeting moiety comprising a VHH, $(VHH)_2$, or scFv that specifically binds to a membrane protein.

[00242] Embodiment 3. A fusion protein comprising an effector moiety comprising a functional fragment of a human deubiquitinase that is capable of mediating deubiquitination that comprises

an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 293, and a targeting moiety comprising a VHH, $(VHH)_2$, or scFv that specifically binds to a membrane protein.

[00243] Embodiment 4. The fusion protein of any one of Embodiments 1-3, wherein said targeting moiety is a VHH or $(VHH)_2$.

[00244] Embodiment 5. The fusion protein of any one of Embodiments 1-4, wherein said membrane protein is GRIN2B, CFTR, SCN1A, ATP7B, KCNQ2, SCN2A, CACNA1A, SLC2A1, SCN8A, PRRT2, GRIN2A, SLC6A1, USH2A, ATP1A2, ATP1A3, SCN9A, PCDH19, GABRB3, TSC2, TSC1, KCNQ3, DMD, RHO, JAG1, ITPR1, SLC50A1, TMEM258, or FSHR.

[00245] Embodiment 6. The fusion protein of any one of Embodiments 1-3, wherein the membrane protein is SCN1A, GRIN2B, SLC50A1, TMEM258, or FSHR.

5.3.5 Methods of Making Fusion Proteins

[00246] Fusion proteins described herein can be made by any conventional technique known in the art, for example, recombinant techniques or chemical synthesis (*e.g.,* solid phase peptide synthesis). In some embodiments, the fusion protein is made through recombinant expression in a cell (e.g., a eukaryotic cell, e.g., a mammalian cell). Briefly, the fusion protein can be made by synthesizing the DNA encoding the fusion protein and cloning the DNA into any suitable expression vector. Numerous cloning vectors are known to those of skill in the art, and the selection of an appropriate cloning vector is a matter of choice. The gene can be placed under the control of a promoter, ribosome binding site (for bacterial expression) and, optionally, an operator and/or one or more enhancer elements, so that the DNA sequence encoding the fusion protein is transcribed into RNA in the host cell transformed by a vector containing this expression construction. The coding sequence may or may not contain a signal peptide or leader sequence. Heterologous leader sequences can be added to the coding sequence that causes the secretion of the expressed polypeptide from the host organism. Other regulatory sequences may also be desirable which allow for regulation of expression of the protein sequences relative to the growth of the host cell. Such regulatory sequences are known to those of skill in the art, and examples include those which cause the expression of a gene to be turned on or off in response to a chemical or physical stimulus, including the presence of a regulatory compound. Other types of regulatory

elements may also be present in the vector, for example, enhancer sequences. The control sequences and other regulatory sequences may be ligated to the coding sequence prior to insertion into a vector, such as the cloning vectors described above. Alternatively, the coding sequence can be cloned directly into an expression vector which already contains the control sequences and an appropriate restriction site.

[00247] The expression vector may then be used to transform an appropriate host cell. A number of mammalian cell lines are known in the art and include immortalized cell lines available from the American Type Culture Collection (ATCC), such as, but not limited to, Chinese hamster ovary (CHO) cells, CHO-suspension cells (CHO-S), HeLa cells, HEK293, baby hamster kidney (BHK) cells, monkey kidney cells (COS), VERO, HepG2, MadinDarby bovine kidney (MDBK) cells, NOS, U2OS, A549, HT1080, CAD, P19, NIH3T3, L929, N2a, MCF-7, Y79, SO-Rb50, DUKX-X11, and J558L.

[00248] Depending on the expression system and host selected, the fusion protein is produced by growing host cells transformed by an expression vector described above under conditions whereby the fusion protein is expressed. The fusion protein is then isolated from the host cells and purified. If the expression system secretes the fusion protein into growth media, the fusion protein can be purified directly from the media. If the fusion protein is not secreted, it is isolated from cell lysates. The selection of the appropriate growth conditions and recovery methods are within the skill of the art. Once purified, the amino acid sequences of the fusion proteins can be determined, i.e., by repetitive cycles of Edman degradation, followed by amino acid analysis by HPLC. Other methods of amino acid sequencing are also known in the art. Once purified, the functionality of the fusion protein can be assessed, *e.g.,* as described herein, *e.g.,* utilizing a bifunctional ELISA.

[00249] As described above, functionality of the fusion protein can be tested by any method known in the art. Each functionality can be measured in a separate assay. For example, binding of the targeting domain to the target protein can be measure using an enzyme linked immunosorbent assay (ELISA). Catalytic activity of the effector domain can be measured using any standard deubiquitinase activity assay known in the art. For example, BioVision Deubiquitinase Activity Assay Kit (Fluorometric) Catalog # K485-100 according to the manufacturer's instructions. The deubiquitinase activity of a fusion protein described herein can be measured for example by using a fluorescent deubiquitinase substrate to detect deubiquitinase activity upon cleavage of the fluorescent substrate. The deubiquitinase activity can also be measured according to the materials

and methods set forth in the Examples provided herein.

5.4 Nucleic Acids, Host Cells, Vectors, and Viral Particles

[00250] In one aspect, provided herein are nucleic acid molecules encoding a fusion protein described herein. In some embodiments, the nucleic acid molecule is a DNA molecule. In some embodiments, the nucleic acid molecule is an RNA molecule. In some embodiments, the nucleic acid molecule contains at least one modified nucleic acid (e.g., that increases stability of the nucleic acid molecule), e.g., phosphorothioate, N6-methyladenosine (m6A), N6,2′-O-dimethyladenosine (m6Am), 8-oxo-7,8-dihydroguanosine (8-oxoG), pseudouridine (Ψ), 5-methylcytidine (m5C), and N4-acetylcytidine (ac4C).

[00251] In one aspect, provided herein is a host cell (or population of host cells) comprising a nucleic acid encoding a fusion protein described herein. In some embodiments, the nucleic acid is incorporated into the genome of the host cell. In some embodiments, the nucleic acid is not incorporated into the genome of the host cell. In some embodiments, the nucleic acid is present in the cell episomally. In some embodiments, the host cell is a human cell. In some embodiments, the host cell is a mammalian cell. In some embodiments, the host cell is a mouse, rat, hamster, guinea pig, cat, dog, or human cell. In some embodiments, the host cell is modified in vitro, ex vivo, or in vivo.

[00252] The nucleic acid can be introduced into the host cell by any suitable method known in the art (e.g., as described herein). For example, a viral delivery system (e.g., a retrovirus, an adenovirus, an adeno associated virus, a herpes virus, a lentivirus, a pox virus, a vaccinia virus, a vesicular stomatitis virus, a polio virus, a Newcastle's Disease virus, an Epstein-Barr virus, an influenza virus, a reoviruses, a myxoma virus, a maraba virus, a rhabdovirus, or a coxsackie virus delivery system) can be utilized to deliver a nucleic acid (e.g., DNA or RNA molecule) encoding the fusion protein for expression with the host cell. In some embodiments, the nucleic acid encoding the fusion protein is present episomally within the host cell. In some embodiments, the nucleic acid encoding the fusion protein is incorporated into the genome of the host cell. In some embodiments, the virus replication competent. In some embodiments, the virus is replication deficient.

[00253] In some embodiments, a nucleic acid (DNA or RNA) is delivered to the host cell using a non-viral vector (e.g., a plasmid) encoding the fusion protein. In some embodiments, the nucleic

acid encoding the fusion protein is present episomally within the host cell. In some embodiments, the nucleic acid encoding the fusion protein is incorporated into the genome of the host cell. Exemplary non-viral transfection methods known in the art include, but are not limited to, direct delivery of DNA such as by ex vivo transfection, by injection (e.g., microinjection), electroporation, liposome mediated transfection, receptor-mediated transfection, microprojectile bombardment, by agitation with silicon carbide fibers Through the application of techniques such as these cells may be stably or transiently transfected with a nucleic acid encoding a fusion protein described herein to express the encoded fusion protein.

[00254] In one aspect, provided herein are vectors comprising a nucleic acid encoding a fusion protein described herein (e.g., a nucleic acid described herein). In some embodiments, the vector is a viral vector. Exemplary viral vectors include, but are not limited to, retroviral vectors, adenoviral vectors, adeno associated viral vectors, herpes viral vectors, lentiviral vectors, pox viral vectors, vaccinia viral vectors, vesicular stomatitis viral vectors, polio viral vectors, Newcastle's Disease viral vectors, Epstein-Barr viral vectors, influenza viral vectors, reovirus vectors, myxoma viral vectors, maraba viral vectors, rhabdoviral vectors, and coxsackie viral vectors. In some embodiments, the vector is a non-viral vector. In some embodiments, the non-viral vector is a plasmid.

[00255] In one aspect, provided herein is a viral particle (or population of viral particles) that comprise a nucleic acid encoding a fusion protein described herein (e.g., a nucleic acid described herein). In some embodiments, the viral particle is an RNA virus. In some embodiments, the viral particle is a DNA virus. In some embodiments, the viral particle comprises a double stranded genome. In some embodiments, the viral particle comprises a single stranded genome. Exemplary viral particles include, but are not limited to, a retrovirus, an adenovirus, an adeno associated virus, a herpes virus, a lentivirus, a pox virus, a vaccinia virus, a vesicular stomatitis virus, a polio virus, a Newcastle's Disease virus, an Epstein-Barr virus, an influenza virus, a reoviruses, a myxoma virus, a maraba virus, a rhabdovirus, or a coxsackie.

5.5 Pharmaceutical Compositions

[00256] In one aspect, provided herein are pharmaceutical compositions comprising 1) a fusion protein described herein, a nucleic acid encoding a fusion protein described herein, a vector comprising a nucleic acid encoding a fusion protein described herein, or a viral particle comprising

a nucleic acid encoding a fusion protein described herein; and 2) at least one pharmaceutically acceptable carrier, excipient, stabilizer buffer, diluent, surfactant, preservative and/or adjuvant, etc (see, e.g., Remington's Pharmaceutical Sciences (1990) Mack Publishing Co., Easton, PA). A person of ordinary skill in the art can select suitable excipient for inclusion in the pharmaceutical composition. For example, the formulation of the pharmaceutical composition may differ based on the route of administration (e.g., intravenous, subcutaneous, etc.), and/or the active molecule contained within the pharmaceutical composition (e.g., a viral particle, a non-viral vector, a nucleic acid not contained within a vector).

[00257] Acceptable carriers, excipients, or stabilizers are preferably nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, or other organic acids; antioxidants including ascorbic acid or methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride, benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol;or m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, or other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (*e.g.,* Zn-protein complexes); and/or non-ionic surfactants such as TWEEN™, PLURONICS™ or polyethylene glycol (PEG).

[00258] In one embodiment, the present disclosure provides a pharmaceutical composition comprising a fusion protein described herein for use as a medicament. In another embodiment, the disclosure provides a pharmaceutical composition for use in a method for the treatment of cancer. In some embodiments, pharmaceutical compositions comprise a fusion protein disclosed herein, and optionally one or more additional prophylactic or therapeutic agents, in a pharmaceutically acceptable carrier.

[00259] A pharmaceutical composition may be formulated for any route of administration to a subject. Specific examples of routes of administration include parenteral administration (*e.g.*, intravenous, subcutaneous, intramuscular). In some embodiments, the pharmaceutical composition is formulated for intravenous administration. In some embodiments, the

pharmaceutical composition is formulated for subcutaneous administration. Injectables can be prepared in conventional forms, either as liquid solutions or suspensions. The injectables can contain one or more excipients. Exemplary excipients include, for example, water, saline, dextrose, glycerol or ethanol. In addition, if desired, the pharmaceutical compositions to be administered can also contain minor amounts of non-toxic auxiliary substances such as wetting or emulsifying agents, pH buffering agents, stabilizers, solubility enhancers, or other such agents, such as for example, sodium acetate, sorbitan monolaurate, triethanolamine oleate or cyclodextrins.

[00260] In some embodiments, the pharmaceutical composition is formulated for intravenous administration. Suitable carriers for intravenous administration include physiological saline or phosphate buffered saline (PBS), or solutions containing thickening or solubilizing agents, such as glucose, polyethylene glycol, or polypropylene glycol or mixtures thereof.

[00261] The compositions to be used for *in vivo* administration can be sterile. This is readily accomplished by filtration through, *e.g.,* sterile filtration membranes.

[00262] Pharmaceutically acceptable carriers used in the parenteral preparations described herein include for example, aqueous vehicles, nonaqueous vehicles, antimicrobial agents, isotonic agents, buffers, antioxidants, local anesthetics, suspending and dispersing agents, emulsifying agents, sequestering or chelating agents or other pharmaceutically acceptable substances. Examples of aqueous vehicles, which can be incorporated in one or more of the formulations described herein, include sodium chloride injection, Ringer's injection, isotonic dextrose injection, sterile water injection, dextrose or lactated Ringer's injection. Nonaqueous parenteral vehicles, which can be incorporated in one or more of the formulations described herein, include fixed oils of vegetable origin, cottonseed oil, corn oil, sesame oil or peanut oil. Antimicrobial agents in bacteriostatic or fungistatic concentrations can be added to the parenteral preparations described herein and packaged in multiple-dose containers, which include phenols or cresols, mercurials, benzyl alcohol, chlorobutanol, methyl and propyl p-hydroxybenzoic acid esters, thimerosal, benzalkonium chloride or benzethonium chloride. Isotonic agents, which can be incorporated in one or more of the formulations described herein, include sodium chloride or dextrose. Buffers, which can be incorporated in one or more of the formulations described herein, include phosphate or citrate. Antioxidants, which can be incorporated in one or more of the formulations described herein, include sodium bisulfate. Local anesthetics, which can be incorporated in one or more of

the formulations described herein, include procaine hydrochloride. Suspending and dispersing agents, which can be incorporated in one or more of the formulations described herein, include sodium carboxymethylcelluose, hydroxypropyl methylcellulose or polyvinylpyrrolidone. Emulsifying agents, which can be incorporated in one or more of the formulations described herein, include Polysorbate 80 (TWEEN® 80). A sequestering or chelating agent of metal ions, which can be incorporated in one or more of the formulations described herein, is EDTA. Pharmaceutical carriers, which can be incorporated in one or more of the formulations described herein, also include ethyl alcohol, polyethylene glycol or propylene glycol for water miscible vehicles; orsodium hydroxide, hydrochloric acid, citric acid or lactic acid for pH adjustment.

[00263] The precise dose to be employed in a pharmaceutical composition will also depend on the route of administration, and the seriousness of the condition caused by it, and should be decided according to the judgment of the practitioner and each subject's circumstances. For example, effective doses may also vary depending upon means of administration, target site, physiological state of the subject (including age, body weight, and health), other medications administered, or whether therapy is prophylactic or therapeutic. Therapeutic dosages are preferably titrated to optimize safety and efficacy.

5.6 Methods of Therapeutic Use

[00264] In one aspect, provided herein are methods of treating a disease in a subject by administering to the subject having the disease a fusion protein described herein, a nucleic acid encoding a fusion protein described herein, a vector comprising a nucleic acid encoding a fusion protein described herein, or a viral particle comprising a nucleic acid encoding a fusion protein described herein.

[00265] The fusion protein can be delivered to host cells via any method known in the art. For example, a viral delivery system (e.g., a retrovirus, an adenovirus, an adeno associated virus, a herpes virus, a lentivirus, a pox virus, a vaccinia virus, a vesicular stomatitis virus, a polio virus, a Newcastle's Disease virus, an Epstein-Barr virus, an influenza virus, a reoviruses, a myxoma virus, a maraba virus, a rhabdovirus, an enadenotucirev or a coxsackie) can be utilized to deliver a nucleic acid (e.g., DNA or RNA molecule) encoding the fusion protein for expression within a population of cells of a subject. In some embodiments, the nucleic acid encoding the fusion protein is present episomally within the population of cells of the subject. In some embodiments, the nucleic acid

encoding the fusion protein is incorporated into the genome of the population of cells of the subject. In some embodiments, the virus is replication competent. In some embodiments, the virus is replication deficient.

[00266] In some embodiments, the fusion protein is administered to the subject. In some embodiments, a nucleic acid (DNA or RNA) is administered to the subject. In some embodiments, the nucleic acid (DNA or RNA) is complexed within a carrier (e.g., a nanoparticle, a liposome, a microsphere). In some embodiments, a nucleic acid (DNA or RNA) within a non-viral vector (e.g., a plasmid) encoding the fusion protein is administered to the subject.

5.6.1 Administration

[00267] The fusion protein can be delivered to host cells via any method known in the art. For example, a viral delivery system (e.g., a retrovirus, an adenovirus, an adeno associated virus, a herpes virus, a lentivirus, a pox virus, a vaccinia virus, a vesicular stomatitis virus, a polio virus, a Newcastle's Disease virus, an Epstein-Barr virus, an influenza virus, a reoviruses, a myxoma virus, a maraba virus, a rhabdovirus, an enadenotucirev or a coxsackie) can be utilized to deliver a nucleic acid (e.g., DNA or RNA molecule) encoding the fusion protein for expression within a population of cells of a subject. In some embodiments, the nucleic acid encoding the fusion protein is present episomally within the population of cells of the subject. In some embodiments, the nucleic acid encoding the fusion protein is incorporated into the genome of the population of cells of the subject. In some embodiments, the virus is replication competent. In some embodiments, the virus is replication deficient.

[00268] In some embodiments, the fusion protein is administered to the subject. In some embodiments, a nucleic acid (DNA or RNA) is administered to the subject. In some embodiments, the nucleic acid (DNA or RNA) is complexed within a carrier (e.g., a nanoparticle, a liposome, a microsphere). In some embodiments, a nucleic acid (DNA or RNA) within a non-viral vector (e.g., a plasmid) encoding the fusion protein is administered to the subject.

[00269] In some embodiment, the fusion protein is administered parenterally. In some embodiments, the fusion protein is administered via intravenous, intramuscular, intraarterial, intrathecal, intralymphatic, intralesional, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal, epidural or intrasternal injection or infusion. In some embodiments, the

fusion protein is intravenously administered. In some embodiments, the fusion protein is subcutaneously administered. In some embodiments, the fusion protein is administered via a non-parenteral route, or orally. Other non-parenteral routes include a topical, epidermal or mucosal route of administration, for example, intranasally, vaginally, rectally, sublingually or topically. Administering can also be performed, for example, once, a plurality of times, and/or over one or more extended periods.

[00270] In some embodiments, the methods disclosed herein are used in place of standard of care therapies. In certain embodiments, a standard of care therapy is used in combination with any method disclosed herein. In some embodiments, the methods disclosed herein are used after standard of care therapy has failed. In some embodiments, the fusion protein is co-administered, administered prior to, or administered after, an additional therapeutic agent. In some embodiments, the disease is a genetic disease.

5.6.2 Exemplary Genetic Diseases

[00271] In some embodiments, the disease is a genetic disease. In some embodiments, the genetic disease is associated with decreased expression of a functional target membrane protein. In some embodiments, the genetic disease is associated with decreased stability of a functional target membrane protein. In some embodiments, the genetic disease is associated with increased ubiquitination of a target membrane protein. In some embodiments, the genetic disease is associated with increased ubiquitination and degradation of a target membrane protein. In some embodiments, the genetic disease is a haploinsufficiency disease.

[00272] In some embodiments, the disease is an epileptic encephalopathy. In some embodiments, the epileptic encephalopathy is an early infantile epileptic encephalopathy. In some embodiments, the early infantile epileptic encephalopathy is selected from the group consisting of early infantile epileptic encephalopathy type 9, early infantile epileptic encephalopathy type 11, early infantile epileptic encephalopathy type 13, and early infantile epileptic encephalopathy type 27. In some embodiments, the disease is an episodic ataxia. In some embodiments, the disease is episodic ataxia type 2. In some embodiments, the disease is an episodic kinesigenic dyskinesia. In some embodiments, the disease is episodic kinesigenic dyskinesia type 1. In some embodiments, the disease is epilepsy. In some embodiments, the epilepsy is focal, with speech disorder and with or without mental retardation; myoclonic-atonic epilepsy; epilepsy type 7; or GABRB3 associated

epilepsy. In some embodiments, the disease is tuberous sclerosis. In some embodiments, the disease is tuberous sclerosis type 1 or tuberous sclerosis type 2. In some embodiments, the disease is KCNQ2 encephalopathy.

[00273] In some embodiments, the disease is selected from the group consisting of early a GRIN2B-Related Disorder, a SCN2A-Related Disorder, a SCN8A-Related Disorder, SLC6A1-Related Disorder, a PRRT2 Dyskinesia & Epilepsy, a GRIN2A-Related Disorder, a CACNA1A-Related Disorder, a SCN9A Epilepsy, a PCDH19 Encephalopathy, KCNQ2 encephalopathy, infantile epileptic encephalopathy type 9, early infantile epileptic encephalopathy type 11, early infantile epileptic encephalopathy type 13, early infantile epileptic encephalopathy type 27, cystic fibrosis, Dravet syndrome, Wilson disease, episodic ataxia type 2; GLUT1 deficiency syndrome, episodic kinesigenic dyskinesia 1, epilepsy (e.g., focal, with speech disorder and with or without mental retardation), myoclonic-atonic epilepsy, Usher syndrome type 2A, alternating hemiplegia of childhood, alternating hemiplegia of childhood type 2, epilepsy type 7, GABRB3 associated epilepsy; tuberous sclerosis type 2; tuberous sclerosis type 1, KCNQ2-Related Disorders (Epileptic Encephalopathy), Becker Muscular Dystrophy, Autosomal Dominant RP, Alagille syndrome 1, Gillespie Syndrome, and Ovarian dysgenesis 1 (ODG1).

[00274] In some embodiments, the target membrane protein is GRIN2B, and the disease is a GRIN2B related disorder (e.g., an epileptic encephalopathy). In some embodiments, the target membrane protein is GRIN2B, and the disease is an early infantile epileptic encephalopathy. In some embodiments, the target membrane protein is GRIN2B, and the disease is early infantile epileptic encephalopathy type 27. In some embodiments, the target membrane protein is CFTR, and the disease is cystic fibrosis. In some embodiments, the target membrane protein is SCN1A, and the disease is Dravet syndrome. In some embodiments, the target membrane protein is ATP7B, and the disease is Wilson disease. In some embodiments, the target membrane protein is CACNA1A, and the disease is a CACA1A related disorder. In some embodiments, the target membrane protein is CACNA1A, and the disease is episodic ataxia type 2. In some embodiments, the target membrane protein is KCNQ2, and the disease is an KCNQ2 encephalopathy. In some embodiments, the target membrane protein is KCNQ2, and the disease is an epileptic encephalopathy. In some embodiments, the target membrane protein is SCN2A, and the disease is a SCN2A related disorder (e.g., an epileptic encephalopathy). In some embodiments, the target membrane protein is SCN2A, and the disease is early infantile epileptic encephalopathy type 11.

In some embodiments, the target membrane protein is SLC2A1, and the disease is GLUT1 deficiency syndrome. In some embodiments, the target membrane protein is SCN8A, and the disease is a SCN8A related disorder (e.g., an epileptic encephalopathy). In some embodiments, the target membrane protein is SCN8A, and the disease is an epileptic encephalopathy. In some embodiments, the target membrane protein is SCN8A, and the disease is early infantile epileptic encephalopathy type 13. In some embodiments, the target membrane protein is PRRT2, and the disease is a PRRPT2 dyskinesia and/or epilepsy. In some embodiments, the target membrane protein is PRRT2, and the disease is an episodic kinesigenic dyskinesia type. In some embodiments, the target membrane protein is PRRT2, and the disease is episodic kinesigenic dyskinesia type 1. In some embodiments, the target membrane protein is GRIN2A, and the disease is a GRIN2A related disorder. In some embodiments, the target membrane protein is GRIN2A, and the disease is epilepsy. In some embodiments, the target membrane protein is GRIN2A, and the disease is focal epilepsy. In some embodiments, the target membrane protein is GRIN2A, and the disease is focal epilepsy with speech disorder and with or without mental retardation. In some embodiments, the target membrane protein is SLC6A1, and the disease is a SLC6A1 related disorder. In some embodiments, the target membrane protein is SLC6A1, and the disease is epilepsy. In some embodiments, the target membrane protein is SLC6A1, and the disease is myoclonic-atonic epilepsy. In some embodiments, the target membrane protein is USH2A, and the disease is Usher syndrome. In some embodiments, the target membrane protein is USH2A, and the disease is Usher syndrome type 2A. In some embodiments, the target membrane protein is ATP1A2, and the disease is alternating hemiplegia of childhood. In some embodiments, the target membrane protein is ATP1A2, and the disease is alternating hemiplegia of childhood type 1. In some embodiments, the target membrane protein is ATP1A3, and the disease is alternating hemiplegia of childhood. In some embodiments, the target membrane protein is ATP1A3, and the disease is alternating hemiplegia of childhood type 2. In some embodiments, the target membrane protein is SCN9A, and the disease an SCN9A epilepsy. In some embodiments, the target membrane protein is SCN9A1, and the disease an SCN9A epilepsy. In some embodiments, the target membrane protein is SCN9A1, and the disease is epilepsy. In some embodiments, the target membrane protein is SCN9A1, and the disease is epilepsy type 7. In some embodiments, the target membrane protein is PCDH19, and the disease is PCDH19 encephalopathy. In some embodiments, the target membrane protein is PCDH19, and the disease is an early infantile epileptic

encephalopathy. In some embodiments, the target membrane protein is PCDH19, and the disease is early infantile epileptic encephalopathy type 9. In some embodiments, the target membrane protein is GABRB3, and the disease is epilepsy. In some embodiments, the target membrane protein is GABRB3, and the disease is GABRB3 associated epilepsy. In some embodiments, the target membrane protein is TSC2, and the disease is tuberous sclerosis. In some embodiments, the target membrane protein is TSC2, and the disease is tuberous sclerosis type 2. In some embodiments, the target membrane protein is TSC2, and the disease is tuberous sclerosis type 1. In some embodiments, the target membrane protein is TSC1, and the disease is tuberous sclerosis. In some embodiments, the target membrane protein is TSC1, and the disease is tuberous sclerosis type 1. In some embodiments, the target membrane protein is TSC1, and the disease is tuberous sclerosis type 2. In some embodiments, the target membrane protein is KCNQ3, and the disease is KCNQ2-Related Disorders (Epileptic Encephalopathy). In some embodiments, the target membrane protein is DMD, and the disease is Becker Muscular Dystrophy. In some embodiments, the target membrane protein is RHO, and the disease is Autosomal Dominant RP. In some embodiments, the target membrane protein is JAG1, and the disease is Alagille syndrome 1. In some embodiments, the target membrane protein is ITPR1, and the disease is Gillespie Syndrome. In some embodiments, the target membrane protein is FSHR, and the disease is ovarian dysgenesis 1 (ODG1).

5.7 Kits

[00275] In one aspect, provided herein are kits comprising a fusion protein described herein, a nucleic acid encoding a fusion protein described herein, a vector comprising a nucleic acid encoding a fusion protein described herein, or a viral particle comprising a nucleic acid encoding a fusion protein described herein, for therapeutic uses. Kits typically include a label indicating the intended use of the contents of the kit and instructions for use. The term label includes any writing, or recorded material supplied on or with the kit, or which otherwise accompanies the kit. Accordingly, this disclosure provides a kit for treating a subject afflicted with a disease (*e.g.*, a genetic disease), the kit comprising: (a) a dosage of a fusion protein, a nucleic acid encoding a fusion protein described herein, a vector comprising a nucleic acid encoding a fusion protein described herein, or a viral particle comprising a nucleic acid encoding a fusion described herein; and (b) instructions for using the fusion protein in any of the therapy methods disclosed herein.

6. EXAMPLES

[00276] The present invention is further illustrated by the following examples which should not be construed as further limiting.

6.1 Example 1. Generation of Targeted Engineered Deubiquitinases

[00277] This example provides general experimental methods of using fluorescent tagged target proteins together with fluorophore tagged engineered deubiquitinases (enDUBs) to demonstrate up-regulation of expression in the context of an enDUB. For illustrative purposes the constructs disclosed below will be synthesized in a suitable vector for mammalian expression. Generally, the target protein will be expressed with a C-terminal YFP followed by a P2A cleavage signal and an mCherry protein as a second reporter (Target protein – YFP – P2A – mCherry). This construct will be co-transfected in the presence of a trifunctional fusion protein comprising of a CFP protein followed by a P2A signal and a nanobody specifically binding to YPF followed by the engineered DUB (CFP – P2A - Anti-YFPnanobody – enDUB). In applications for drug treatment the targeting nanobodies (or other specific binders) will be directed to the wild type (or disease-causing mutant) protein in the cell to be upregulated while the enDUB is fused to a binding protein directed to the target protein. Target protein binding moieties could be any antibody or antibody fragments, nanobodies, or any other non-antibody scaffold such as fibronectins, anticalins, ankyrin repeats or natural binding proteins interacting specifically with the target protein to be upregulated. The amino acid sequence of the components of the test fusion proteins is provided in Table 4 below.

Table 4. Amino Acid Sequence of Components of test fusion proteins

Description	SEQ ID NO	Amino Acid Sequence
Target Proteins		
Beta 2 adrenergic receptor human	246	MGQPGNGSAFLLAPNGSHAPDHDVTQERDEVWVVGMGIVMSLIVLA IVFGNVLVITAIAKFERLQTVTNYFITSLACADLVMGLAVVPFGAA HILMKMWTFGNFWCEFWTSIDVLCVTASIETLCVIAVDRYFAITSP FKYQSLLTKNKARVIILMVWIVSGLTSFLPIQMHWYRATHQEAINC YANETCCDFFTNQAYAIASSIVSFYVPLVIMVFVYSRVFQEAKRQL QKIDKSEGRFHVQNLSQVEQDGRTGHGLRRSSKFCLKEHKALKTLG IIMGTFTLCWLPFFIVNIVHVIQDNLIRKEVYILLNWIGYVNSGFN PLIYCRSPDFRIAFQELLCLRRSSLKAYGNGYSSNGNTGEQSGYHV EQEKENKLLCEDLPGTEDFVGHQGTVPSDNIDSQGRNCSTNDSLL
Kappa-type opioid receptor human	247	MDSPIQIFRGEPGPTCAPSACLPPNSSAWFPGWAEPDSNGSAGSED AQLEPAHISPAIPVIITAVYSVVFVVGLVGNSLVMFVIIRYTKMKT ATNIYIFNLALADALVTTTMPFQSTVYLMNSWPFGDVLCKIVISID

		YYNMFTSIFTLTMMSVDRYIAVCHPVKALDFRTPLKAKIINICIWL LSSSVGISAIVLGGTKVREDVDVIECSLQFPDDDYSWWDLFMKICV FIFAFVIPVLIIIVCYTLMILRLKSVRLLSGSREKDRNLRRITRLV LVVVAVFVVCWTPIHIFILVEALGSTSHSTAALSSYYFCIALGYTN SSLNPILYAFLDENFKRCFRDFCFPLKMRMERQSTSRVRNTVQDPA YLRDIDGMNKPV
Muscarinic acetylcholine receptor M2 human	248	MNNSTNSSNNSLALTSPYKTFEVVFIVLVAGSLSLVTIIGNILVMV SIKVNRHLQTVNNYFLFSLACADLIIGVFSMNLYTLYTVIGYWPLG PVVCDLWLALDYVVSNASVMNLLIISFDRYFCVTKPLTYPVKRTTK MAGMMIAAAWVLSFILWAPAILFWQFIVGVRTVEDGECYIQFFSNA AVTFGTAIAAFYLPVIIMTVLYWHISRASKSRIKKDKKEPVANQDP VSPSLVQGRIVKPNNNNMPSSDDGLEHNKIQNGKAPRDPVTENCVQ GEEKESSNDSTSVSAVASNMRDDEITQDENTVSTSLGHSKDENSKQ TCIRIGTKTPKSDSCTPTNTTVEVVGSSGQNGDEKQNIVARKIVKM TKQPAKKKPPPSREKKVTRTILAILLAFIITWAPYNVMVLINTFCA PCIPNTVWTIGYWLCYINSTINPACYALCNATFKKTFKHLLMCHYK NIGATR
Fluorescent Proteins		
YFP	249	VSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLKF ICTTGKLPVPWPTLVTTFGYGLQCFARYPDHMKQHDFFKSAMPEGY VQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNILG HKLEYNYNSHNVYIMADKQKNGIKVNFKIRHNIEDGSVQLADHYQQ NTPIGDGPVLLPDNHYLSYQSALSKDPNEKRDHMVLLEFVTAAGIT LGMDELYK
mCherry	250	MVSKGEEDNMAIIKEFMRFKVHMEGSVNGHEFEIEGEGEGRPYEGT QTAKLKVTKGGPLPFAWDILSPQFMYGSKAYVKHPADIPDYLKLSF PEGFKWERVMNFEDGGVVTVTQDSSLQDGEFIYKVKLRGTNFPSDG PVMQKKTMGWEASSERMYPEDGALKGEIKQRLKLKDGGHYDAEVKT TYKAKKPVQLPGAYNVNIKLDITSHNEDYTIVEQYERAEGRHSTGG MDELYK
CFP	251	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYK
A2 Peptides		
P2A	252	GSGATNFSLLKQAGDVEENPGP
T2A	253	GSGEGRGSLLTCGDVEENPGP
E2A	254	GSGQCTNYALLKLAGDVESNPGP
Target Binders		
YFP targeting nanobody	255	QVQLVESGGALVQPGGSLRLSCAASGFPVNRYSMRWYRQAPGKERE WVAGMSSAGDRSSYEDSVKGRFTISRDDARNTVYLQMNSLKPEDTA VYYCNVNVGFEYWGQGTQVTVSS

Beta 2 adrenergic receptor human binder (monobody)	256	QVQLQESGGGLVQAGGSLRLSCAASGSIFALNIMGWYRQAPGKQRE LVAAIHSGGTTNYANSVKGRFTISRDNAANTVYLQMNSLKPEDTAV YYCNVKDFGAIIYDYDYWGQGTQVTVSS
Kappa-type opioid receptor human binder (monobody)	257	MAQVQLVESGGGLVRPGGSLRLSCVDSERTSYPMGWFRRAPGKERE FVASITWSGIDPTYADSVADRFTTSRDVANNTLYLQMNSLKHEDTA VYYCAARAPVGQSSSPYDYDYWGQGTQVTVSSHHHHHHEPEA
Muscarinic acetylcholine receptor M2 human (monobody)	258	GPGSQVQLQESGGGLVQAGDSLRLSCAASGFDFDNFDDYAIGWFRQ APGQEREGVSCIDPSDGSTIYADSAKGRFTISSDNAENTVYLQMNS LKPEDTAVYVCSAWTLFHSDEYWGQGTQVTVSS
EnDUBS		
Cezanne	259	PPSFSEGSGGSRTPEKGFSDREPTRPPRPILQRQDDIVQEKRLSRG ISHASSSIVSLARSHVSSNGGGGGSNEHPLEMPICAFQLPDLTVYN EDFRSFIERDLIEQSMLVALEQAGRLNWWVSVDPTSQRLLPLATTG DGNCLLHAASLGMWGFHDRDLMLRKALYALMEKGVEKEALKRRWRW QQTQQNKESGLVYTEDEWQKEWNELIKLASSEPRMHLGTNGANCGG VESSEEPVYESLEEFHVFVLAHVLRRPIVVVADTMLRDSGGEAFAP IPFGGIYLPLEVPASQCHRSPLVLAYDQAHFSALVSMEQKENTKEQ AVIPLTDSEYKLLPLHFAVDPGKGWEWGKDDSDNVRLASVILSLEV KLHLLHSYMNVKWIPLSSDAQAPLAQ
OTUD1	260	DEKLALYLAEVEKQDKYLRQRNKYRFHIIPDGNCLYRAVSKTVYGD QSLHRELREQTVHYIADHLDHFSPLIEGDVGEFIIAAAQDGAWAGY PELLAMGQMLNVNIHLTTGGRLESPTVSTMIHYLGPEDSLRPSIWL SWLSNGHYDAVFDHSYPNPEYDNWCKQTQVQRKRDEELAKSMAISL SKMYIEQNACS
TRABID	261	LEVDFKKLKQIKNRMKKTDWLFLNACVGVVEGDLAAIEAYKSSGGD IARQLTADEVRLLNRPSAFDVGYTLVHLAIRFQRQDMLAILLTEVS QQAAKCIPAMVCPELTEQIRREIAASLHQRKGDFACYFLTDLVTFT LPADIEDLPPTVQEKLFDEVLDRDVQKELEEESPIINWSLELATRL DSRLYALWNRTAGDCLLDSVLQATWGIYDKDSVLRKALHDSLHDCS HWFYTRWKDWESWYSQSFGLHFSLREEQWQEDWAFILSLASQPGAS LEQTHIFVLAHILRRPIIVYGVKYYKSFRGETLGYTRFQGVYLPLL WEQSFCWKSPIALGYTRGHFSALVAMENDGYGNRGAGANLNTDDDV TITFLPLVDSERKLLHVHFLSAQELGNEEQQEKLLREWLDCCVTEG GVLVAMQKSSRRRNHPLVTQMVEKWLDRYRQIRPCTSLS
USP21	262	SDDKMAHHTLLLGSGHVGLRNLGNTCFLNAVLQCLSSTRPLRDFCL RRDFRQEVPGGGRAQELTEAFADVIGALWHPDSCEAVNPTRFRAVF QKYVPSFSGYSQQDAQEFLKLLMERLHLEINRRGRRAPPILANGPV PSPPRRGGALLEEPELSDDDRANLMWKRYLEREDSKIVDLFVGQLK SCLKCQACGYRSTTFEVFCDLSLPIPKKGFAGGKVSLRDCFNLFTK EEELESENAPVCDRCRQKTRSTKKLTVQRFPRILVLHLNRFSASRG SIKKSSVGVDFPLQRLSLGDFASDKAGSPVYQLYALCNHSGSVHYG HYTALCRCQTGWHVYNDSRVSPVSENQVASSEGYVLFYQLMQEPPR CL

OTUD4	263	ATPMDAYLRKLGLYRKLVAKDGSCLFRAVAEQVLHSQSRHVEVRMA CIHYLRENREKFEAFIEGSFEEYLKRLENPQEWVGQVEISALSLMY RKDFIIYREPNVSPSQVTENNFPEKVLLCFSNGNHYDIVYPIKYKE SSAMCQSLLYELLYEKVFKTDVSKIVMELDTLEVADE
Human USP3 (full length) nuclear located	264	MECPHLSSSVCIAPDSAKFPNGSPSSWCCSVCRSNKSPWVCLTCSS VHCGRYVNGHAKKHYEDAQVPLTNHKKSEKQDKVQHTVCMDCSSYS TYCYRCDDFVVNDTKLGLVQKVREHLQNLENSAFTADRHKKRKLLE NSTLNSKLLKVNGSTTAICATGLRNLGNTCFMNAILQSLSNIEQFC CYFKELPAVELRNGKTAGRRTYHTRSQGDNNVSLVEEFRKTLCALW QGSQTAFSPESLFYVVWKIMPNFRGYQQQDAHEFMRYLLDHLHLEL QGGFNGVSRSAILQENSTLSASNKCCINGASTVVTAIFGGILQNEV NCLICGTESRKFDPFLDLSLDIPSQFRSKRSKNQENGPVCSLRDCL RSFTDLEELDETELYMCHKCKKKQKSTKKFWIQKLPKVLCLHLKRF HWTAYLRNKVDTYVEFPLRGLDMKCYLLEPENSGPESCLYDLAAVV VHHGSGVGSGHYTAYATHEGRWFHFNDSTVTLTDEETVVKAKAYIL FYVEHQAKAGSDKL

[00278] The amino acid sequence of the test fusion proteins is provided in Table 5 below.

Table 5. Amino acid sequence of exemplary test fusion proteins

Description	SEQ ID NO	Amino Acid Sequence
Beta 2 adrenergic receptor human Target – YFP-P2A – mCherrry	265	MGQPGNGSAFLLAPNGSHAPDHDVTQERDEVWVVGMGIVMSLIVLA IVFGNVLVITAIAKFERLQTVTNYFITSLACADLVMGLAVVPFGAA HILMKMWTFGNFWCEFWTSIDVLCVTASIETLCVIAVDRYFAITSP FKYQSLLTKNKARVIILMVWIVSGLTSFLPIQMHWYRATHQEAINC YANETCCDFFTNQAYAIASSIVSFYVPLVIMVFVYSRVFQEAKRQL QKIDKSEGRFHVQNLSQVEQDGRTGHGLRRSSKFCLKEHKALKTLG IIMGTFTLCWLPFFIVNIVHVIQDNLIRKEVYILLNWIGYVNSGFN PLIYCRSPDFRIAFQELLCLRRSSLKAYGNGYSSNGNTGEQSGYHV EQEKENKLLCEDLPGTEDFVGHQGTVPSDNIDSQGRNCSTNDSLLV SKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLKFI CTTGKLPVPWPTLVTTFGYGLQCFARYPDHMKQHDFFKSAMPEGYV QERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNILGH KLEYNYNSHNVYIMADKQKNGIKVNFKIRHNIEDGSVQLADHYQQN TPIGDGPVLLPDNHYLSYQSALSKDPNEKRDHMVLLEFVTAAGITL GMDELYKGSGATNFSLLKQAGDVEENPGPMVSKGEEDNMAIIKEFM RFKVHMEGSVNGHEFEIEGEGEGRPYEGTQTAKLKVTKGGPLPFAW DILSPQFMYGSKAYVKHPADIPDYLKLSFPEGFKWERVMNFEDGGV VTVTQDSSLQDGEFIYKVKLRGTNFPSDGPVMQKKTMGWEASSERM YPEDGALKGEIKQRLKLKDGGHYDAEVKTTYKAKKPVQLPGAYNVN IKLDITSHNEDYTIVEQYERAEGRHSTGGMDELYK
Human kappa-type opioid receptor Target – YFP- P2A – mCherrry	266	MDSPIQIFRGEPGPTCAPSACLPPNSSAWFPGWAEPDSNGSAGSED AQLEPAHISPAIPVIITAVYSVVFVVGLVGNSLVMFVIIRYTKMKT ATNIYIFNLALADALVTTTMPFQSTVYLMNSWPFGDVLCKIVISID YYNMFTSIFTLTMMSVDRYIAVCHPVKALDFRTPLKAKIINICIWL LSSSVGISAIVLGGTKVREDVDVIECSLQFPDDDYSWWDLFMKICV FIFAFVIPVLIIIVCYTLMILRLKSVRLLSGSREKDRNLRRITRLV LVVVAVFVVCWTPIHIFILVEALGSTSHSTAALSSYYFCIALGYTN SSLNPILYAFLDENFKRCFRDFCFPLKMRMERQSTSRVRNTVQDPA YLRDIDGMNKPVVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGE

		GDATYGKLTLKFICTTGKLPVPWPTLVTTFGYGLQCFARYPDHMKQ HDFFKSAMPEGYVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELK GIDFKEDGNILGHKLEYNYNSHNVYIMADKQKNGIKVNFKIRHNIE DGSVQLADHYQQNTPIGDGPVLLPDNHYLSYQSALSKDPNEKRDHM VLLEFVTAAGITLGMDELYKGSGATNFSLLKQAGDVEENPGPMVSK GEEDNMAIIKEFMRFKVHMEGSVNGHEFEIEGEGEGRPYEGTQTAK LKVTKGGPLPFAWDILSPQFMYGSKAYVKHPADIPDYLKLSFPEGF KWERVMNFEDGGVVTVTQDSSLQDGEFIYKVKLRGTNFPSDGPVMQ KKTMGWEASSERMYPEDGALKGEIKQRLKLKDGGHYDAEVKTTYKA KKPVQLPGAYNVNIKLDITSHNEDYTIVEQYERAEGRHSTGGMDEL YK
Muscarinic acetylcholine receptor M2 Target – YFP-P2A – mCherrry	267	MNNSTNSSNNSLALTSPYKTFEVVFIVLVAGSLSLVTIIGNILVMV SIKVNRHLQTVNNYFLFSLACADLIIGVFSMNLYTLYTVIGYWPLG PVVCDLWLALDYVVSNASVMNLLIISFDRYFCVTKPLTYPVKRTTK MAGMMIAAAWVLSFILWAPAILFWQFIVGVRTVEDGECYIQFFSNA AVTFGTAIAAFYLPVIIMTVLYWHISRASKSRIKKDKKEPVANQDP VSPSLVQGRIVKPNNNNMPSSDDGLEHNKIQNGKAPRDPVTENCVQ GEEKESSNDSTSVSAVASNMRDDEITQDENTVSTSLGHSKDENSKQ TCIRIGTKTPKSDSCTPTNTTVEVVGSSGQNGDEKQNIVARKIVKM TKQPAKKKPPPSREKKVTRTILAILLAFIITWAPYNVMVLINTFCA PCIPNTVWTIGYWLCYINSTINPACYALCNATFKKTFKHLLMCHYK NIGATRVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYG KLTLKFICTTGKLPVPWPTLVTTFGYGLQCFARYPDHMKQHDFFKS AMPEGYVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKE DGNILGHKLEYNYNSHNVYIMADKQKNGIKVNFKIRHNIEDGSVQL ADHYQQNTPIGDGPVLLPDNHYLSYQSALSKDPNEKRDHMVLLEFV TAAGITLGMDELYKGSGATNFSLLKQAGDVEENPGPMVSKGEEDNM AIIKEFMRFKVHMEGSVNGHEFEIEGEGEGRPYEGTQTAKLKVTKG GPLPFAWDILSPQFMYGSKAYVKHPADIPDYLKLSFPEGFKWERVM NFEDGGVVTVTQDSSLQDGEFIYKVKLRGTNFPSDGPVMQKKTMGW EASSERMYPEDGALKGEIKQRLKLKDGGHYDAEVKTTYKAKKPVQL PGAYNVNIKLDITSHNEDYTIVEQYERAEGRHSTGGMDELYK
CFP- P2A-Cezanne enDUB	268	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPPPSFSEGSGGSRTPE KGFSDREPTRPPRPILQRQDDIVQEKRLSRGISHASSSIVSLARSH VSSNGGGGGSNEHPLEMPICAFQLPDLTVYNEDFRSFIERDLIEQS MLVALEQAGRLNWWVSVDPTSQRLLPLATTGDGNCLLHAASLGMWG FHDRDLMLRKALYALMEKGVEKEALKRRWRWQQTQQNKESGLVYTE DEWQKEWNELIKLASSEPRMHLGTNGANCGGVESSEEPVYESLEEF HVFVLAHVLRRPIVVVADTMLRDSGGEAFAPIPFGGIYLPLEVPAS QCHRSPLVLAYDQAHFSALVSMEQKENTKEQAVIPLTDSEYKLLPL HFAVDPGKGWEWGKDDSDNVRLASVILSLEVKLHLLHSYMNVKWIP LSSDAQAPLAQ
CFP- P2A-OTUD1 enDUB	269	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ

		QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPDEKLALYLAEVEKQD KYLRQRNKYRFHIIPDGNCLYRAVSKTVYGDQSLHRELREQTVHYI ADHLDHFSPLIEGDVGEFIIAAAQDGAWAGYPELLAMGQMLNVNIH LTTGGRLESPTVSTMIHYLGPEDSLRPSIWLSWLSNGHYDAVFDHS YPNPEYDNWCKQTQVQRKRDEELAKSMAISLSKMYIEQNACS
CFP- P2A-TRABID enDUB	270	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPLEVDFKKLKQIKNRM KKTDWLFLNACVGVVEGDLAAIEAYKSSGGDIARQLTADEVRLLNR PSAFDVGYTLVHLAIRFQRQDMLAILLTEVSQQAAKCIPAMVCPEL TEQIRREIAASLHQRKGDFACYFLTDLVTFTLPADIEDLPPTVQEK LFDEVLDRDVQKELEEESPIINWSLELATRLDSRLYALWNRTAGDC LLDSVLQATWGIYDKDSVLRKALHDSLHDCSHWFYTRWKDWESWYS QSFGLHFSLREEQWQEDWAFILSLASQPGASLEQTHIFVLAHILRR PIIVYGVKYYKSFRGETLGYTRFQGVYLPLLWEQSFCWKSPIALGY TRGHFSALVAMENDGYGNRGAGANLNTDDDVTITFLPLVDSERKLL HVHFLSAQELGNEEQQEKLLREWLDCCVTEGGVLVAMQKSSRRRNH PLVTQMVEKWLDRYRQIRPCTSLS
CFP- P2A-USP21 enDUB	271	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPSDDKMAHHTLLLGSG HVGLRNLGNTCFLNAVLQCLSSTRPLRDFCLRRDFRQEVPGGGRAQ ELTEAFADVIGALWHPDSCEAVNPTRFRAVFQKYVPSFSGYSQQDA QEFLKLLMERLHLEINRRGRRAPPILANGPVPSPPRRGGALLEEPE LSDDDRANLMWKRYLEREDSKIVDLFVGQLKSCLKCQACGYRSTTF EVFCDLSLPIPKKGFAGGKVSLRDCFNLFTKEEELESENAPVCDRC RQKTRSTKKLTVQRFPRILVLHLNRFSASRGSIKKSSVGVDFPLQR LSLGDFASDKAGSPVYQLYALCNHSGSVHYGHYTALCRCQTGWHVY NDSRVSPVSENQVASSEGYVLFYQLMQEPPRCL
CFP- P2A-OTUD4 enDUB	272	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPATPMDAYLRKLGLYR KLVAKDGSCLFRAVAEQVLHSQSRHVEVRMACIHYLRENREKFEAF IEGSFEEYLKRLENPQEWVGQVEISALSLMYRKDFIIYREPNVSPS QVTENNFPEKVLLCFSNGNHYDIVYPIKYKESSAMCQSLLYELLYE KVFKTDVSKIVMELDTLEVADE
CFP-P2A-a-YFPnanobody-Cezanne enDUB	273	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI

		TLGMDELYKGSGATNFSLLKQAGDVEENPGPQVQLVESGGALVQPG GSLRLSCAASGFPVNRYSMRWYRQAPGKEREWVAGMSSAGDRSSYE DSVKGRFTISRDDARNTVYLQMNSLKPEDTAVYYCNVNVGFEYWGQ GTQVTVSSPPSFSEGSGGSRTPEKGFSDREPTRPPRPILQRQDDIV QEKRLSRGISHASSSIVSLARSHVSSNGGGGGSNEHPLEMPICAFQ LPDLTVYNEDFRSFIERDLIEQSMLVALEQAGRLNWWVSVDPTSQR LLPLATTGDGNCLLHAASLGMWGFHDRDLMLRKALYALMEKGVEKE ALKRRWRWQQTQQNKESGLVYTEDEWQKEWNELIKLASSEPRMHLG TNGANCGGVESSEEPVYESLEEFHVFVLAHVLRRPIVVVADTMLRD SGGEAFAPIPFGGIYLPLEVPASQCHRSPLVLAYDQAHFSALVSME QKENTKEQAVIPLTDSEYKLLPLHFAVDPGKGWEWGKDDSDNVRLA SVILSLEVKLHLLHSYMNVKWIPLSSDAQAPLAQ
CFP-P2A-a-YFPnanobody-OTUD1 enDUB	274	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPQVQLVESGGALVQPG GSLRLSCAASGFPVNRYSMRWYRQAPGKEREWVAGMSSAGDRSSYE DSVKGRFTISRDDARNTVYLQMNSLKPEDTAVYYCNVNVGFEYWGQ GTQVTVSSDEKLALYLAEVEKQDKYLRQRNKYRFHIIPDGNCLYRA VSKTVYGDQSLHRELREQTVHYIADHLDHFSPLIEGDVGEFIIAAA QDGAWAGYPELLAMGQMLNVNIHLTTGGRLESPTVSTMIHYLGPED SLRPSIWLSWLSNGHYDAVFDHSYPNPEYDNWCKQTQVQRKRDEEL AKSMAISLSKMYIEQNACS
CFP-P2A-a-YFPnanobody-TRABID enDUB	275	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPQVQLVESGGALVQPG GSLRLSCAASGFPVNRYSMRWYRQAPGKEREWVAGMSSAGDRSSYE DSVKGRFTISRDDARNTVYLQMNSLKPEDTAVYYCNVNVGFEYWGQ GTQVTVSSLEVDFKKLKQIKNRMKKTDWLFLNACVGVVEGDLAAIE AYKSSGGDIARQLTADEVRLLNRPSAFDVGYTLVHLAIRFQRQDML AILLTEVSQQAAKCIPAMVCPELTEQIRREIAASLHQRKGDFACYF LTDLVTFTLPADIEDLPPTVQEKLFDEVLDRDVQKELEEESPIINW SLELATRLDSRLYALWNRTAGDCLLDSVLQATWGIYDKDSVLRKAL HDSLHDCSHWFYTRWKDWESWYSQSFGLHFSLREEQWQEDWAFILS LASQPGASLEQTHIFVLAHILRRPIIVYGVKYYKSFRGETLGYTRF QGVYLPLLWEQSFCWKSPIALGYTRGHFSALVAMENDGYGNRGAGA NLNTDDDVTITFLPLVDSERKLLHVHFLSAQELGNEEQQEKLLREW LDCCVTEGGVLVAMQKSSRRRNHPLVTQMVEKWLDRYRQIRPCTSL
CFP-P2A-a-YFPnanobody-USP21 enDUB	276	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPQVQLVESGGALVQPG GSLRLSCAASGFPVNRYSMRWYRQAPGKEREWVAGMSSAGDRSSYE DSVKGRFTISRDDARNTVYLQMNSLKPEDTAVYYCNVNVGFEYWGQ

		GTQVTVSSSDDKMAHHTLLLGSGHVGLRNLGNTCFLNAVLQCLSST RPLRDFCLRRDFRQEVPGGGRAQELTEAFADVIGALWHPDSCEAVN PTRFRAVFQKYVPSFSGYSQQDAQEFLKLLMERLHLEINRRGRRAP PILANGPVPSPPRRGGALLEEPELSDDDRANLMWKRYLEREDSKIV DLFVGQLKSCLKCQACGYRSTTFEVFCDLSLPIPKKGFAGGKVSLR DCFNLFTKEEELESENAPVCDRCRQKTRSTKKLTVQRFPRILVLHL NRFSASRGSIKKSSVGVDFPLQRLSLGDFASDKAGSPVYQLYALCN HSGSVHYGHYTALCRCQTGWHVYNDSRVSPVSENQVASSEGYVLFY QLMQEPPRCL
CFP-P2A-a-YFPnanobody-OTUD4 enDUB	277	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPQVQLVESGGALVQPG GSLRLSCAASGFPVNRYSMRWYRQAPGKEREWVAGMSSAGDRSSYE DSVKGRFTISRDDARNTVYLQMNSLKPEDTAVYYCNVNVGFEYWGQ GTQVTVSSATPMDAYLRKLGLYRKLVAKDGSCLFRAVAEQVLHSQS RHVEVRMACIHYLRENREKFEAFIEGSFEEYLKRLENPQEWVGQVE ISALSLMYRKDFIIYREPNVSPSQVTENNFPEKVLLCFSNGNHYDI VYPIKYKESSAMCQSLLYELLYEKVFKTDVSKIVMELDTLEVADE
CFP-P2A -anti-beta 2 adrenergic receptor targeting binder-Cezanne enDUB	278	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPQVQLQESGGGLVQAG GSLRLSCAASGSIFALNIMGWYRQAPGKQRELVAAIHSGGTTNYAN SVKGRFTISRDNAANTVYLQMNSLKPEDTAVYYCNVKDFGAIIYDY DYWGQGTQVTVSSPPSFSEGSGGSRTPEKGFSDREPTRPPRPILQR QDDIVQEKRLSRGISHASSSIVSLARSHVSSNGGGGGSNEHPLEMP ICAFQLPDLTVYNEDFRSFIERDLIEQSMLVALEQAGRLNWWVSVD PTSQRLLPLATTGDGNCLLHAASLGMWGFHDRDLMLRKALYALMEK GVEKEALKRRWRWQQTQQNKESGLVYTEDEWQKEWNELIKLASSEP RMHLGTNGANCGGVESSEEPVYESLEEFHVFVLAHVLRRPIVVVAD TMLRDSGGEAFAPIPFGGIYLPLEVPASQCHRSPLVLAYDQAHFSA LVSMEQKENTKEQAVIPLTDSEYKLLPLHFAVDPGKGWEWGKDDSD NVRLASVILSLEVKLHLLHSYMNVKWIPLSSDAQAPLAQ
CFP-P2A -anti-beta 2 adrenergic receptor targeting binder-OTUD1 enDUB	279	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPQVQLQESGGGLVQAG GSLRLSCAASGSIFALNIMGWYRQAPGKQRELVAAIHSGGTTNYAN SVKGRFTISRDNAANTVYLQMNSLKPEDTAVYYCNVKDFGAIIYDY DYWGQGTQVTVSSDEKLALYLAEVEKQDKYLRQRNKYRFHIIPDGN CLYRAVSKTVYGDQSLHRELREQTVHYIADHLDHFSPLIEGDVGEF IIAAAQDGAWAGYPELLAMGQMLNVNIHLTTGGRLESPTVSTMIHY LGPEDSLRPSIWLSWLSNGHYDAVFDHSYPNPEYDNWCKQTQVQRK RDEELAKSMAISLSKMYIEQNACS

CFP-P2A -anti-beta 2 adrenergic receptor targeting binder-TRABID enDUB	280	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPQVQLQESGGGLVQAG GSLRLSCAASGSIFALNIMGWYRQAPGKQRELVAAIHSGGTTNYAN SVKGRFTISRDNAANTVYLQMNSLKPEDTAVYYCNVKDFGAIIYDY DYWGQGTQVTVSSLEVDFKKLKQIKNRMKKTDWLFLNACVGVVEGD LAAIEAYKSSGGDIARQLTADEVRLLNRPSAFDVGYTLVHLAIRFQ RQDMLAILLTEVSQQAAKCIPAMVCPELTEQIRREIAASLHQRKGD FACYFLTDLVTFTLPADIEDLPPTVQEKLFDEVLDRDVQKELEEES PIINWSLELATRLDSRLYALWNRTAGDCLLDSVLQATWGIYDKDSV LRKALHDSLHDCSHWFYTRWKDWESWYSQSFGLHFSLREEQWQEDW AFILSLASQPGASLEQTHIFVLAHILRRPIIVYGVKYYKSFRGETL GYTRFQGVYLPLLWEQSFCWKSPIALGYTRGHFSALVAMENDGYGN RGAGANLNTDDDVTITFLPLVDSERKLLHVHFLSAQELGNEEQQEK LLREWLDCCVTEGGVLVAMQKSSRRRNHPLVTQMVEKWLDRYRQIR PCTSLS
CFP-P2A -anti-beta 2 adrenergic receptor targeting binder-USP21 enDUB	281	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNF QVQLQESGGGLVQAGGSLRLSCAASGSIFALNIMGWYRQAPGKQRE LVAAIHSGGTTNYANSVKGRFTISRDNAANTVYLQMNSLKPEDTAV YYCNVKDFGAIIYDYDYWGQGTQVTVSSSDDKMAHHTLLLGSGHVG LRNLGNTCFLNAVLQCLSSTRPLRDFCLRRDFRQEVPGGGRAQELT EAFADVIGALWHPDSCEAVNPTRFRAVFQKYVPSFSGYSQQDAQEF LKLLMERLHLEINRRGRRAPPILANGPVPSPPRRGGALLEEPELSD DDRANLMWKRYLEREDSKIVDLFVGQLKSCLKCQACGYRSTTFEVF CDLSLPIPKKGFAGGKVSLRDCFNLFTKEEELESENAPVCDRCRQK TRSTKKLTVQRFPRILVLHLNRFSASRGSIKKSSVGVDFPLQRLSL GDFASDKAGSPVYQLYALCNHSGSVHYGHYTALCRCQTGWHVYNDS RVSPVSENQVASSEGYVLFYQLMQEPPRCL
CFP-P2A -anti-beta 2 adrenergic receptor targeting binder-OTUD4 enDUB	282	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPQVQLQESGGGLVQAG GSLRLSCAASGSIFALNIMGWYRQAPGKQRELVAAIHSGGTTNYAN SVKGRFTISRDNAANTVYLQMNSLKPEDTAVYYCNVKDFGAIIYDY DYWGQGTQVTVSSATPMDAYLRKLGLYRKLVAKDGSCLFRAVAEQV LHSQSRHVEVRMACIHYLRENREKFEAFIEGSFEEYLKRLENPQEW VGQVEISALSLMYRKDFIIYREPNVSPSQVTENNFPEKVLLCFSNG NHYDIVYPIKYKESSAMCQSLLYELLYEKVFKTDVSKIVMELDTLE VADE
CFP-P2A -anti-Kappa-type	283	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG

opioid receptor targeting binder-Cezanne enDUB		YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPMAQVQLVESGGGLVR PGGSLRLSCVDSERTSYPMGWFRRAPGKEREFVASITWSGIDPTYA DSVADRFTTSRDVANNTLYLQMNSLKHEDTAVYYCAARAPVGQSSS PYDYDYWGQGTQVTVSSHHHHHHEPEAPPSFSEGSGGSRTPEKGFS DREPTRPPRPILQRQDDIVQEKRLSRGISHASSSIVSLARSHVSSN GGGGGSNEHPLEMPICAFQLPDLTVYNEDFRSFIERDLIEQSMLVA LEQAGRLNWWVSVDPTSQRLLPLATTGDGNCLLHAASLGMWGFHDR DLMLRKALYALMEKGVEKEALKRRWRWQQTQQNKESGLVYTEDEWQ KEWNELIKLASSEPRMHLGTNGANCGGVESSEEPVYESLEEFHVFV LAHVLRRPIVVVADTMLRDSGGEAFAPIPFGGIYLPLEVPASQCHR SPLVLAYDQAHFSALVSMEQKENTKEQAVIPLTDSEYKLLPLHFAV DPGKGWEWGKDDSDNVRLASVILSLEVKLHLLHSYMNVKWIPLSSD AQAPLAQ
CFP-P2A -anti-Kappa-type opioid receptor targeting binder-OTUD1 enDUB	284	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPMAQVQLVESGGGLVR PGGSLRLSCVDSERTSYPMGWFRRAPGKEREFVASITWSGIDPTYA DSVADRFTTSRDVANNTLYLQMNSLKHEDTAVYYCAARAPVGQSSS PYDYDYWGQGTQVTVSSHHHHHHEPEADEKLALYLAEVEKQDKYLR QRNKYRFHIIPDGNCLYRAVSKTVYGDQSLHRELREQTVHYIADHL DHFSPLIEGDVGEFIIAAAQDGAWAGYPELLAMGQMLNVNIHLTTG GRLESPTVSTMIHYLGPEDSLRPSIWLSWLSNGHYDAVFDHSYPNP EYDNWCKQTQVQRKRDEELAKSMAISLSKMYIEQNACS
CFP-P2A -anti-Kappa-type opioid receptor targeting binder-TRABID enDUB	285	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPMAQVQLVESGGGLVR PGGSLRLSCVDSERTSYPMGWFRRAPGKEREFVASITWSGIDPTYA DSVADRFTTSRDVANNTLYLQMNSLKHEDTAVYYCAARAPVGQSSS PYDYDYWGQGTQVTVSSHHHHHHEPEALEVDFKKLKQIKNRMKKTD WLFLNACVGVVEGDLAAIEAYKSSGGDIARQLTADEVRLLNRPSAF DVGYTLVHLAIRFQRQDMLAILLTEVSQQAAKCIPAMVCPELTEQI RREIAASLHQRKGDFACYFLTDLVTFTLPADIEDLPPTVQEKLFDE VLDRDVQKELEEESPIINWSLELATRLDSRLYALWNRTAGDCLLDS VLQATWGIYDKDSVLRKALHDSLHDCSHWFYTRWKDWESWYSQSFG LHFSLREEQWQEDWAFILSLASQPGASLEQTHIFVLAHILRRPIIV YGVKYYKSFRGETLGYTRFQGVYLPLLWEQSFCWKSPIALGYTRGH FSALVAMENDGYGNRGAGANLNTDDDVTITFLPLVDSERKLLHVHF LSAQELGNEEQQEKLLREWLDCCVTEGGVLVAMQKSSRRRNHPLVT QMVEKWLDRYRQIRPCTSLS
CFP-P2A -anti-Kappa-type opioid receptor	286	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL

targeting binder-USP21 enDUB		GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPMAQVQLVESGGGLVR PGGSLRLSCVDSERTSYPMGWFRRAPGKEREFVASITWSGIDPTYA DSVADRFTTSRDVANNTLYLQMNSLKHEDTAVYYCAARAPVGQSSS PYDYDYWGQGTQVTVSSHHHHHHEPEASDDKMAHHTLLLGSGHVGL RNLGNTCFLNAVLQCLSSTRPLRDFCLRRDFRQEVPGGGRAQELTE AFADVIGALWHPDSCEAVNPTRFRAVFQKYVPSFSGYSQQDAQEFL KLLMERLHLEINRRGRRAPPILANGPVPSPPRRGGALLEEPELSDD DRANLMWKRYLEREDSKIVDLFVGQLKSCLKCQACGYRSTTFEVFC DLSLPIPKKGFAGGKVSLRDCFNLFTKEEELESENAPVCDRCRQKT RSTKKLTVQRFPRILVLHLNRFSASRGSIKKSSVGVDFPLQRLSLG DFASDKAGSPVYQLYALCNHSGSVHYGHYTALCRCQTGWHVYNDSR VSPVSENQVASSEGYVLFYQLMQEPPRCL
CFP-P2A -anti-Kappa-type opioid receptor targeting binder-OTUD4 enDUB	287	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPMAQVQLVESGGGLVR PGGSLRLSCVDSERTSYPMGWFRRAPGKEREFVASITWSGIDPTYA DSVADRFTTSRDVANNTLYLQMNSLKHEDTAVYYCAARAPVGQSSS PYDYDYWGQGTQVTVSSHHHHHHEPEAATPMDAYLRKLGLYRKLVA KDGSCLFRAVAEQVLHSQSRHVEVRMACIHYLRENREKFEAFIEGS FEEYLKRLENPQEWVGQVEISALSLMYRKDFIIYREPNVSPSQVTE NNFPEKVLLCFSNGNHYDIVYPIKYKESSAMCQSLLYELLYEKVFK TDVSKIVMELDTLEVADE
CFP-P2A -anti-Muscarinic acetylcholine receptor M2 targeting binder-Cezanne enDUB	288	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPGPGSQVQLQESGGGL VQAGDSLRLSCAASGFDFDNFDDYAIGWFRQAPGQEREGVSCIDPS DGSTIYADSAKGRFTISSDNAENTVYLQMNSLKPEDTAVYVCSAWT LFHSDEYWGQGTQVTVSSPPSFSEGSGGSRTPEKGFSDREPTRPPR PILQRQDDIVQEKRLSRGISHASSSIVSLARSHVSSNGGGGGSNEH PLEMPICAFQLPDLTVYNEDFRSFIERDLIEQSMLVALEQAGRLNW WVSVDPTSQRLLPLATTGDGNCLLHAASLGMWGFHDRDLMLRKALY ALMEKGVEKEALKRRWRWQQTQQNKESGLVYTEDEWQKEWNELIKL ASSEPRMHLGTNGANCGGVESSEEPVYESLEEFHVFVLAHVLRRPI VVVADTMLRDSGGEAFAPIPFGGIYLPLEVPASQCHRSPLVLAYDQ AHFSALVSMEQKENTKEQAVIPLTDSEYKLLPLHFAVDPGKGWEWG KDDSDNVRLASVILSLEVKLHLLHSYMNVKWIPLSSDAQAPLAQ
CFP-P2A -anti-Muscarinic acetylcholine receptor M2 targeting binder-OTUD1 enDUB	289	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPGPGSQVQLQESGGGL VQAGDSLRLSCAASGFDFDNFDDYAIGWFRQAPGQEREGVSCIDPS

		DGSTIYADSAKGRFTISSDNAENTVYLQMNSLKPEDTAVYVCSAWT LFHSDEYWGQGTQVTVSSDEKLALYLAEVEKQDKYLRQRNKYRFHI IPDGNCLYRAVSKTVYGDQSLHRELREQTVHYIADHLDHFSPLIEG DVGEFIIAAAQDGAWAGYPELLAMGQMLNVNIHLTTGGRLESPTVS TMIHYLGPEDSLRPSIWLSWLSNGHYDAVFDHSYPNPEYDNWCKQT QVQRKRDEELAKSMAISLSKMYIEQNACS
CFP-P2A -anti-Muscarinic acetylcholine receptor M2 targeting binder-TRABID enDUB	290	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPGPGSQVQLQESGGGL VQAGDSLRLSCAASGFDFDNFDDYAIGWFRQAPGQEREGVSCIDPS DGSTIYADSAKGRFTISSDNAENTVYLQMNSLKPEDTAVYVCSAWT LFHSDEYWGQGTQVTVSSLEVDFKKLKQIKNRMKKTDWLFLNACVG VVEGDLAAIEAYKSSGGDIARQLTADEVRLLNRPSAFDVGYTLVHL AIRFQRQDMLAILLTEVSQQAAKCIPAMVCPELTEQIRREIAASLH QRKGDFACYFLTDLVTFTLPADIEDLPPTVQEKLFDEVLDRDVQKE LEEESPIINWSLELATRLDSRLYALWNRTAGDCLLDSVLQATWGIY DKDSVLRKALHDSLHDCSHWFYTRWKDWESWYSQSFGLHFSLREEQ WQEDWAFILSLASQPGASLEQTHIFVLAHILRRPIIVYGVKYYKSF RGETLGYTRFQGVYLPLLWEQSFCWKSPIALGYTRGHFSALVAMEN DGYGNRGAGANLNTDDDVTITFLPLVDSERKLLHVHFLSAQELGNE EQQEKLLREWLDCCVTEGGVLVAMQKSSRRRNHPLVTQMVEKWLDR YRQIRPCTSLS
CFP-P2A -anti-Muscarinic acetylcholine receptor M2 targeting binder-USP21 enDUB	291	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPGPGSQVQLQESGGGL VQAGDSLRLSCAASGFDFDNFDDYAIGWFRQAPGQEREGVSCIDPS DGSTIYADSAKGRFTISSDNAENTVYLQMNSLKPEDTAVYVCSAWT LFHSDEYWGQGTQVTVSSSDDKMAHHTLLLGSGHVGLRNLGNTCFL NAVLQCLSSTRPLRDFCLRRDFRQEVPGGGRAQELTEAFADVIGAL WHPDSCEAVNPTRFRAVFQKYVPSFSGYSQQDAQEFLKLLMERLHL EINRRGRRAPPILANGPVPSPPRRGGALLEEPELSDDDRANLMWKR YLEREDSKIVDLFVGQLKSCLKCQACGYRSTTFEVFCDLSLPIPKK GFAGGKVSLRDCFNLFTKEEELESENAPVCDRCRQKTRSTKKLTVQ RFPRILVLHLNRFSASRGSIKKSSVGVDFPLQRLSLGDFASDKAGS PVYQLYALCNHSGSVHYGHYTALCRCQTGWHVYNDSRVSPVSENQV ASSEGYVLFYQLMQEPPRCL
CFP-P2A -anti-Muscarinic acetylcholine receptor M2 targeting binder-OTUD4 enDUB	292	MVSKGEELFTGVVPILVELDGDVNGHKFSVSGEGEGDATYGKLTLK FICTTGKLPVPWPTLVTTLTWGVQCFSRYPDHMKQHDFFKSAMPEG YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNIL GHKLEYNYISHNVYITADKQKNGIKANFKIRHNIEDGSVQLADHYQ QNTPIGDGPVLLPDNHYLSTQSALSKDPNEKRDHMVLLEFVTAAGI TLGMDELYKGSGATNFSLLKQAGDVEENPGPGPGSQVQLQESGGGL VQAGDSLRLSCAASGFDFDNFDDYAIGWFRQAPGQEREGVSCIDPS DGSTIYADSAKGRFTISSDNAENTVYLQMNSLKPEDTAVYVCSAWT LFHSDEYWGQGTQVTVSSATPMDAYLRKLGLYRKLVAKDGSCLFRA

		VAEQVLHSQSRHVEVRMACIHYLRENREKFEAFIEGSFEEYLKRLE NPQEWVGQVEISALSLMYRKDFIIYREPNVSPSQVTENNFPEKVLL CFSNGNHYDIVYPIKYKESSAMCQSLLYELLYEKVFKTDVSKIVME LDTLEVADE

6.2 Example 2. Testing of Targeted Engineered Deubiquitinases

[00279] To demonstrate upregulation of a target protein in the context of a specific targeting enDUB the following experiments will be performed.

Schematic constructs used:

- Control experiment using non-targeting enDUB fusion
    - Target – YFP- P2A – mCherrry
    - CFP- P2A- enDUB (nontargeting control enDUB)
- Test constructs for up-regulation:
    - Target- YFP-P2A-mCherry
    - CFP-P2A-a-YFPnanobody-enDUB
- Or specific targeting enDUB fusion composed of
    - CFP-P2A -anti-targeting binder-enDUB

[00280] Co-transfection of both plasmids carrying the YFP tagged target protein together with the enDUB fused to a target binding protein into HEK cells will be performed. A control construct carrying the enDUB in the absence of the targeting binder will also be co-transfected together with the labeled target protein. After 24-48 hours the transfected cells will be analyzed by FACS or upregulation over the control. The mCherry signal on the target protein will be used to normalize for transfection efficiency while the CFP signal will be used to normalize for the transfection efficiency of the enDUB constructs. The YFP fused to the target protein is the read-out for target gene expression and will be plotted vs the signal in the control transfection. Relative increase in the YFP fluorescence over control will demonstrate upregulation in the presence of the enDUB.

6.3 Example 3. Screening Assay for Testing Fusion Proteins

[00281] The following example describes an assay to analyze the ability of a targeted engineered deubiquitinase (enDub) (e.g., an enDub described herein) to increase expression of a target protein. Generally, the assay involves tagging the target protein with a fluorescent tag (e.g., NanoLuciferase (NLuc)) and an alfa-tag (α-Tag); and tagging a fusion protein of the enDub and

an anti-alfa Tag nanobody with a different fluorescent tag (e.g., Firefly Luciferase (FLuc)) through a cleavable linker. The use of two different fluorescent tags enables normalization of the signal to compensate for variation in transfection/expression, as the second fluorescent tag is rapidly cleaved from the enDub-anti-alfa tag fusion protein inside the cell through cleavage of the cleavable linker. FIG. 2 provides a general schematic of the cellular aspects of the assay. The protocol, including materials and methods is described below.

[00282] CHO-K1 cells were digested with 0.25% (w/v) Trypsin-EDTA, at 37°C, for 5min. Complete medium was added for the CHO-K1 cell cultures to stop the digestion. The CHO-K1 cells were centrifuges at 800 rpm for 5 minutes. After centrifugation, the supernatant was discarded and the CHO-K1 cells were resuspend in 2 mL culture medium and counted. 10^6 CHO-K1 cells were electroporated under 440V with 0.5ug of a plasmid encoding the target protein tagged with NLuc and alfa-tag, and 1ug of a plasmid encoding a) enDub-anti-alfa tag nanobody-FLuc fusion protein (experimental), b) the enDub (control), or the anti-alfa tag nanobody (control). 5E+4 cells/well were placed in in 24 well plates and cultured for 24h, at 37°C, 5% CO_2. The cells were digested with 0.25% (w/v) Trypsin-EDTA, at 37°C for 5min. Complete medium was added to the culture to stop the digestion and the cells were counted for use in NanoGlo® Dual Luciferase® Assay (Promega), which enables detection of FLuc and NLuc® in a single sample. The NanoGlo® Dual Luciferase® Assay was carried out according to manufacturer's instructions (Promega, Nano-Glo® Dual-Luciferase® Reporter Assay Technical Manual #TM426). Briefly, 1E+4 cells/well were placed in 96 well black plates and cultured for 24h, at 37°C, 5% CO_2. The plates were removed from the incubator and allowed to equilibrate to room temperature. The samples were modified as needed to have a starting volume of 80µl per well. All sample wells were injected with 80µl of ONE-Glo™ EX Reagent and incubated for 3 minutes. The firefly luminescence was read in all sample wells using a 1-second integration time. All sample wells were injected with 80µl of NanoDLR™ Stop & Glo® Reagent; and incubated for 5 minutes. The NanoLuc® luminescence of all sample wells was read using a 1-second integration time. The dispensing lines were cleaned according to manufacturer's instructions (Nano-Glo® Dual-Luciferase® Reporter Assay Technical Manual #TM426.) and the data analyzed.

[00283] The amino acid sequence of the components of the fusion proteins used in the assay are detailed in Table 6 below.

Table 6. Amino acid sequence of components of test fusion proteins

Description		SEQ ID NO	Amino Acid Sequence
Fluorescent Protein	NanoLuc	425	VFTLEDFVGDWRQTAGYNLDQVLEQGGVSSLFQ NLGVSVTPIQRIVLSGENGLKIDIHVIIPYEGL SGDQMGQIEKIFKVVYPVDDHHFKVILHYGTLV IDGVTPNMIDYFGRPYEGIAVFDGKKITVTGTL WNGNKIIDERLINPDGSLLFRVTINGVTGWRLC ERILA
	Firefly Luciferase	426	MEDAKNIKKGPAPFYPLEDGTAGEQLHKAMKRY ALVPGTIAFTDAHIEVDITYAEYFEMSVRLAEA MKRYGLNTNHRIVVCSENSLQFFMPVLGALFIG VAVAPANDIYNERELLNSMGISQPTVVFVSKKG LQKILNVQKKLPIIQKIIIMDSKTDYQGFQSMY TFVTSHLPPGFNEYDFVPESFDRDKTIALIMNS SGSTGLPKGVALPHRTACVRFSHARDPIFGNQI IPDTAILSVVPFHHGFGMFTTLGYLICGFRVVL MYRFEEELFLRSLQDYKIQSALLVPTLFSFFAK STLIDKYDLSNLHEIASGGAPLSKEVGEAVAKR FHLPGIRQGYGLTETTSAILITPEGDDKPGAVG KVVPFFEAKVVDLDTGKTLGVNQRGELCVRGPM IMSGYVNNPEATNALIDKDGWLHSGDIAYWDED EHFFIVDRLKSLIKYKGYQVAPAELESILLQHP NIFDAGVAGLPDDDAGELPAAVVVLEHGKTMTE KEIVDYVASQVTTAKKLRGGVVFVDEVPKGLTG KLDARKIREILIKAKKGGKIAVTRLK
Alfa Tag		427	PSRLEEELRRRLTEP
P2A		428	GSGATNFSLLKQAGDVEENPGP
Cezanne (Exemplary Catalytic Domain)		429	PPSFSEGSGGSRTPEKGFSDREPTRPPRPILQR QDDIVQEKRLSRGISHASSSIVSLARSHVSSNG GGGGSNEHPLEMPICAFQLPDLTVYNEDFRSFI ERDLIEQSMLVALEQAGRLNWWVSVDPTSQRLL PLATTGDGNCLLHAASLGMWGFHDRDLMLRKAL YALMEKGVEKEALKRRWRWQQTQQNKESGLVYT EDEWQKEWNELIKLASSEPRMHLGTNGANCGGV ESSEEPVYESLEEFHVFVLAHVLRRPIVVVADT MLRDSGGEAFAPIPFGGIYLPLEVPASQCHRSP LVLAYDQAHFSALVSMEQKENTKEQAVIPLTDS EYKLLPLHFAVDPGKGWEWGKDDSDNVRLASVI LSLEVKLHLLHSYMNVKWIPLSSDAQAPLAQ

[00284] The amino acid sequence of exemplary target fusion proteins comprising a target protein, NLuc, and the alfa tag are detailed in Table 7 below.

Table 7. Amino Acid Sequence of exemplary Target Protein – NLuc – Alfa Tag Fusion Proteins

Test Protein	SEQ ID NO	Amino Acid Sequence
GRIN2A-nanoluc-alfa-tag-fusion	430	MGRVGYWTLLVLPALLVWRGPAPSAAAEKGPPALNIAVMLGHSHD VTERELRTLWGPEQAAGLPLDVNVVALLMNRTDPKSLITHVCDLM SGARIHGLVFGDDTDQEAVAQMLDFISSHTFVPILGIHGGASMIM ADKDPTSTFFQFGASIQQQATVMLKIMQDYDWHVFSLVTTIFPGY REFISFVKTTVDNSFVGWDMQNVITLDTSFEDAKTQVQLKKIHSS

		VILLYCSKDEAVLILSEARSLGLTGYDFFWIVPSLVSGNTELIPK EFPSGLISVSYDDWDYSLEARVRDGIGILTTAASSMLEKFSYIPE AKASCYGQMERPEVPMHTLHPFMVNVTWDGKDLSFTEEGYQVHPR LVVIVLNKDREWEKVGKWENHTLSLRHAVWPRYKSFSDCEPDDNH LSIVTLEEAPFVIVEDIDPLTETCVRNTVPCRKFVKINNSTNEGM NVKKCCKGFCIDILKKLSRTVKFTYDLYLVTNGKHGKKVNNVWNG MIGEVVYQRAVMAVGSLTINEERSEVVDFSVPFVETGISVMVSRS NGTVSPSAFLEPFSASVWVMMFVMLLIVSAIAVFVFEYFSPVGYN RNLAKGKAPHGPSFTIGKAIWLLWGLVFNNSVPVQNPKGTTSKIM VSVWAFFAVIFLASYTANLAAFMIQEEFVDQVTGLSDKKFQRPHD YSPPFRFGTVPNGSTERNIRNNYPYMHQYMTKFNQKGVEDALVSL KTGKLDAFIYDAAVLNYKAGRDEGCKLVTIGSGYIFATTGYGIAL QKGSPWKRQIDLALLQFVGDGEMEELETLWLTGICHNEKNEVMSS QLDIDNMAGVFYMLAAAMALSLITFIWEHLFYWKLRFCFTGVCSD RPGLLFSISRGIYSCIHGVHIEEKKKSPDFNLTGSQSNMLKLLRS AKNISSMSNMNSSRMDSPKRAADFIQRGSLIMDMVSDKGNLMYSD NRSFQGKESIFGDNMNELQTFVANRQKDNLNNYVFQGQHPLTLNE SNPNTVEVAVSTESKANSRPRQLWKKSVDSIRQDSLSQNPVSQRD EATAENRTHSLKSPRYLPEEMAHSDISETSNRATCHREPDNSKNH KTKDNFKRSVASKYPKDCSEVERTYLKTKSSSPRDKIYTIDGEKE PGFHLDPPQFVENVTLPENVDFPDPYQDPSENFRKGDSTLPMNRN PLHNEEGLSNNDQYKLYSKHFTLKDKGSPHSETSERYRQNSTHCR SCLSNMPTYSGHFTMRSPFKCDACLRMGNLYDIDEDQMLQETGNP ATGEQVYQQDWAQNNALQLQKNKLRISRQHSYDNIVDKPRELDLS RPSRSISLKDRERLLEGNFYGSLFSVPSSKLSGKKSSLFPQGLED SKRSKSLLPDHTSDNPFLHSHRDDQRLVIGRCPSDPYKHSLPSQA VNDSYLRSSLRSTASYCSRDSRGHNDVYISEHVMPYAANKNNMYS TPRVLNSCSNRRVYKKMPSIESDVKVPVFTLEDFVGDWRQTAGYN LDQVLEQGGVSSLFQNLGVSVTPIQRIVLSGENGLKIDIHVIIPY EGLSGDQMGQIEKIFKVVYPVDDHHFKVILHYGTLVIDGVTPNMI DYFGRPYEGIAVFDGKKITVTGTLWNGNKIIDERLINPDGSLLFR VTINGVTGWRLCERILAGGGGSPSRLEEELRRRLTEP
SLC2A1-nanoluc-alfa-tag-fusion	431	MEPSSKKLTGRLMLAVGGAVLGSLQFGYNTGVINAPQKVIEEFYN QTWVHRYGESILPTTLTTLWSLSVAIFSVGGMIGSFSVGLFVNRF GRRNSMLMMNLLAFVSAVLMGFSKLGKSFEMLILGRFIIGVYCGL TTGFVPMYVGEVSPTALRGALGTLHQLGIVVGILIAQVFGLDSIM GNKDLWPLLLSIIFIPALLQCIVLPFCPESPRFLLINRNEENRAK SVLKKLRGTADVTHDLQEMKEESRQMMREKKVTILELFRSPAYRQ PILIAVVLQLSQQLSGINAVFYYSTSIFEKAGVQQPVYATIGSGI VNTAFTVVSLFVVERAGRRTLHLIGLAGMAGCAILMTIALALLEQ LPWMSYLSIVAIFGFVAFFEVGPGPIPWFIVAELFSQGPRPAAIA VAGFSNWTSNFIVGMCFQYVEQLCGPYVFIIFTVLLVLFFIFTYF KVPETKGRTFDEIASGFRQGGASQSDKTPEELFHPLGADSQVKVP VFTLEDFVGDWRQTAGYNLDQVLEQGGVSSLFQNLGVSVTPIQRI VLSGENGLKIDIHVIIPYEGLSGDQMGQIEKIFKVVYPVDDHHFK VILHYGTLVIDGVTPNMIDYFGRPYEGIAVFDGKKITVTGTLWNG NKIIDERLINPDGSLLFRVTINGVTGWRLCERILAGGGGSPSRLE EELRRRLTEP
CACNA1A-nanoluc-alfa-tag-fusion	432	MARFGDEMPARYGGGGSGAAAGVVVGSGGGRGAGGSRQGGQPGAQ RMYKQSMAQRARTMALYNPIPVRQNCLTVNRSLFLFSEDNVVRKY AKKITEWPPFEYMILATIIANCIVLALEQHLPDDDKTPMSERLDD

		TEPYFIGIFCFEAGIKIIALGFAFHKGSYLRNGWNVMDFVVVLTG ILATVGTEFDLRTLRAVRVLRPLKLVSGIPSLQVVLKSIMKAMIP LLQIGLLLFFAILIFAIIGLEFYMGKFHTTCFEEGTDDIQGESPA PCGTEEPARTCPNGTKCQPYWEGPNNGITQFDNILFAVLTVFQCI TMEGWTDLLYNSNDASGNTWNWLYFIPLIIIGSFFMLNLVLGVLS GEFAKERERVENRRAFLKLRRQQQIERELNGYMEWISKAEEVILA EDETDGEQRHPFDALRRTTIKKSKTDLLNPEEAEDQLADIASVGS PFARASIKSAKLENSTFFHKKERRMRFYIRRMVKTQAFYWTVLSL VALNTLCVAIVHYNQPEWLSDFLYYAEFIFLGLFMSEMFIKMYGL GTRPYFHSSFNCFDCGVIIGSIFEVIWAVIKPGTSFGISVLRALR LLRIFKVTKYWASLRNLVVSLLNSMKSIISLLFLLFLFIVVFALL GMQLFGGQFNFDEGTPPTNFDTFPAAIMTVFQILTGEDWNEVMYD GIKSQGGVQGGMVFSIYFIVLTLFGNYTLLNVFLAIAVDNLANAQ ELTKDEQEEEEAANQKLALQKAKEVAEVSPLSAANMSIAVKEQQK NQKPAKSVWEQRTSEMRKQNLLASREALYNEMDPDERWKAAYTRH LRPDMKTHLDRPLVVDPQENRNNNTNKSRAAEPTVDQRLGQQRAE DFLRKQARYHDRARDPSGSAGLDARRPWAGSQEAELSREGPYGRE SDHHAREGSLEQPGFWEGEAERGKAGDPHRRHVHRQGGSRESRSG SPRTGADGEHRRHRAHRRPGEEGPEDKAERRARHREGSRPARGGE GEGEGPDGGERRRRHRHGAPATYEGDARREDKERRHRRRKENQGS GVPVSGPNLSTTRPIQQDLGRQDPPLAEDIDNMKNNKLATAESAA PHGSLGHAGLPQSPAKMGNSTDPGPMLAIPAMATNPQNAASRRTP NNPGNPSNPGPPKTPENSLIVTNPSGTQTNSAKTARKPDHTTVDI PPACPPPLNHTVVQVNKNANPDPLPKKEEEKKEEEEDDRGEDGPK PMPPYSSMFILSTTNPLRRLCHYILNLRYFEMCILMVIAMSSIAL AAEDPVQPNAPRNNVLRYFDYVFTGVFTFEMVIKMIDLGLVLHQG AYFRDLWNILDFIVVSGALVAFAFTGNSKGKDINTIKSLRVLRVL RPLKTIKRLPKLKAVFDCVVNSLKNVFNILIVYMLFMFIFAVVAV QLFKGKFFHCTDESKEFEKDCRGKYLLYEKNEVKARDREWKKYEF HYDNVLWALLTLFTVSTGEGWPQVLKHSVDATFENQGPSPGYRME MSIFYVVYFVVFPFFFVNIFVALIIITFQEQGDKMMEEYSLEKNE RACIDFAISAKPLTRHMPQNKQSFQYRMWQFVVSPPFEYTIMAMI ALNTIVLMMKFYGASVAYENALRVFNIVFTSLFSLECVLKVMAFG ILNYFRDAWNIFDFVTVLGSITDILVTEFGNNFINLSFLRLFRAA RLIKLLRQGYTIRILLWTFVQSFKALPYVCLLIAMLFFIYAIIGM QVFGNIGIDVEDEDSDEDEFQITEHNNFRTFFQALMLLFRSATGE AWHNIMLSCLSGKPCDKNSGILTRECGNEFAYFYFVSFIFLCSFL MLNLFVAVIMDNFEYLTRDSSILGPHHLDEYVRVWAEYDPAAWGR MPYLDMYQMLRHMSPPLGLGKKCPARVAYKRLLRMDLPVADDNTV HFNSTLMALIRTALDIKIAKGGADKQQMDAELRKEMMAIWPNLSQ KTLDLLVTPHKSTDLTVGKIYAAMMIMEYYRQSKAKKLQAMREEQ DRTPLMFQRMEPPSPTQEGGPGQNALPSTQLDPGGALMAHESGLK ESPSWVTQRAQEMFQKTGTWSPEQGPPTDMPNSQPNSQSVEMREM GRDGYSDSEHYLPMEGQGRAASMPRLPAENQRRRGRPRGNNLSTI SDTSPMKRSASVLGPKARRLDDYSLERVPPEENQRHHQRRRDRSH RASERSLGRYTDVDTGLGTDLSMTTQSGDLPSKERDQERGRPKDR KHRQHHHHHHHHHHPPPPDKDRYAQERPDHGRARARDQRWSRSPS EGREHMAHRQGSSSVSGSPAPSTSGTSTPRRGRRQLPQTPSTPRP HVSYSPVIRKAGGSGPPQQQQQQQQQQQQQAVARPGRAATSGPRR YPGPTAEPLAGDRPPTGGHSSGRSPRMERRVPGPARSESPRACRH GGARWPASGPHVSEGPPGPRHHGYYRGSDYDEADGPGSGGGEEAM

		AGAYDAPPPVRHASSGATGRSPRTPRASGPACASPSRHGRRLPNG YYPAHGLARPRGPGSRKGLHEPYSESDDDWCKVPVFTLEDFVGDW RQTAGYNLDQVLEQGGVSSLFQNLGVSVTPIQRIVLSGENGLKID IHVIIPYEGLSGDQMGQIEKIFKVVYPVDDHHFKVILHYGTLVID GVTPNMIDYFGRPYEGIAVFDGKKITVTGTLWNGNKIIDERLINP DGSLLFRVTINGVTGWRLCERILAGGGGSPSRLEEELRRRLTEP
GABRB3-nanoluc-alfa-tag-fusion	433	MWGLAGGRLFGIFSAPVLVAVVCCAQSVNDPGNMSFVKETVDKLL KGYDIRLRPDFGGPPVCVGMNIDIASIDMVSEVNMDYTLTMYFQQ YWRDKRLAYSGIPLNLTLDNRVADQLWVPDTYFLNDKKSFVHGVT VKNRMIRLHPDGTVLYGLRITTTAACMMDLRRYPLDEQNCTLEIE SYGYTTDDIEFYWRGGDKAVTGVERIELPQFSIVEHRLVSRNVVF ATGAYPRLSLSFRLKRNIGYFILQTYMPSILITILSWVSFWINYD ASAARVALGITTVLTMTTINTHLRETLPKIPYVKAIDMYLMGCFV FVFLALLEYAFVNYIFFGRGPQRQKKLAEKTAKAKNDRSKSESNR VDAHGNILLTSLEVHNEMNEVSGGIGDTRNSAISFDNSGIQYRKQ SMPREGHGRFLGDRSLPHKKTHLRRRSSQLKIKIPDLTDVNAIDR WSRIVFPFTFSLFNLVYWLYYVNKVPVFTLEDFVGDWRQTAGYNL DQVLEQGGVSSLFQNLGVSVTPIQRIVLSGENGLKIDIHVIIPYE GLSGDQMGQIEKIFKVVYPVDDHHFKVILHYGTLVIDGVTPNMID YFGRPYEGIAVFDGKKITVTGTLWNGNKIIDERLINPDGSLLFRV TINGVTGWRLCERILAGGGGSPSRLEEELRRRLTEP
SLC6A1-nanoluc-alfa-tag-fusion	434	MATNGSKVADGQISTEVSEAPVANDKPKTLVVKVQKKAADLPDRD TWKGRFDFLMSCVGYAIGLGNVWRFPYLCGKNGGGAFLIPYFLTL IFAGVPLFLLECSLGQYTSIGGLGVWKLAPMFKGVGLAAAVLSFW LNIYYIVIISWAIYYLYNSFTTTLPWKQCDNPWNTDRCFSNYSMV NTTNMTSAVVEFWERNMHQMTDGLDKPGQIRWPLAITLAIAWILV YFCIWKGVGWTGKVVYFSATYPYIMLIILFFRGVTLPGAKEGILF YITPNFRKLSDSEVWLDAATQIFFSYGLGLGSLIALGSYNSFHNN VYRDSIIVCCINSCTSMFAGFVIFSIVGFMAHVTKRSIADVAASG PGLAFLAYPEAVTQLPISPLWAILFFSMLLMLGIDSQFCTVEGFI TALVDEYPRLLRNRRELFIAAVCIISYLIGLSNITQGGIYVFKLF DYYSASGMSLLFLVFFECVSISWFYGVNRFYDNIQEMVGSRPCIW WKLCWSFFTPIIVAGVFIFSAVQMTPLTMGNYVFPKWGQGVGWLM ALSSMVLIPGYMAYMFLTLKGSLKQRIQVMVQPSEDIVRPENGPE QPQAGSSTSKEAYIKVPVFTLEDFVGDWRQTAGYNLDQVLEQGGV SSLFQNLGVSVTPIQRIVLSGENGLKIDIHVIIPYEGLSGDQMGQ IEKIFKVVYPVDDHHFKVILHYGTLVIDGVTPNMIDYFGRPYEGI AVFDGKKITVTGTLWNGNKIIDERLINPDGSLLFRVTINGVTGWR LCERILAGGGGSPSRLEEELRRRLTEP
KCNQ2-nanoluc-alfa-tag-fusion	435	MVQKSRNGGVYPGPSGEKKLKVGFVGLDPGAPDSTRDGALLIAGS EAPKRGSILSKPRAGGAGAGKPPKRNAFYRKLQNFLYNVLERPRG WAFIYHAYVFLLVFSCLVLSVFSTIKEYEKSSEGALYILEIVTIV VFGVEYFVRIWAAGCCCRYRGWRGRLKFARKPFCVIDIMVLIASI AVLAAGSQGNVFATSALRSLRFLQILRMIRMDRRGGTWKLLGSVV YAHSKELVTAWYIGFLCLILASFLVYLAEKGENDHFDTYADALWW GLITLTTIGYGDKYPQTWNGRLLAATFTLIGVSFFALPAGILGSG FALKVQEQHRQKHFEKRRNPAAGLIQSAWRFYATNLSRTDLHSTW QYYERTVTVPMYSSQTQTYGASRLIPPLNQLELLRNLKSKSGLAF RKDPPPEPSPSKGSPCRGPLCGCCPGRSSQKVSLKDRVFSSPRGV AAKGKGSPQAQTVRRSPSADQSLEDSPSKVPKSWSFGDRSRARQA FRIKGAASRQNSEEASLPGEDIVDDKSCPCEFVTEDLTPGLKVSI

		RAVCVMRFLVSKRKFKESLRPYDVMDVIEQYSAGHLDMLSRIKSL QSRVDQIVGRGPAITDKDRTKGPAEAELPEDPSMMGRLGKVEKQV LSMEKKLDFLVNIYMQRMGIPPTETEAYFGAKEPEPAPPYHSPED SREHVDRHGCIVKIVRSSSSTGQKNFSAPPAAPPVQCPPSTSWQP QSHPRQGHGTSPVGDHGSLVRIPPPPAHERSLSAYGGGNRASMEF LRQEDTPGCRPPEGNLRDSDTSISIPSVDHEELERSFSGFSISQS KENLDALNSCYAAVAPCAKVRPYIAEGESDTDSDLCTPCGPPPRS ATGEGPFGDVGWAGPRKKVPVFTLEDFVGDWRQTAGYNLDQVLEQ GGVSSLFQNLGVSVTPIQRIVLSGENGLKIDIHVIIPYEGLSGDQ MGQIEKIFKVVYPVDDHHFKVILHYGTLVIDGVTPNMIDYFGRPY EGIAVFDGKKITVTGTLWNGNKIIDERLINPDGSLLFRVTINGVT GWRLCERILAGGGGSPSRLEEELRRRLTEP
SCN8A-nanoluc-alfa-tag-fusion	436	MAARLLAPPGPDSFKPFTPESLANIERRIAESKLKKPPKADGSHR EDDEDSKPKPNSDLEAGKSLPFIYGDIPQGLVAVPLEDFDPYYLT QKTFVVLNRGKTLFRFSATPALYILSPFNLIRRIAIKILIHSVFS MIIMCTILTNCVFMTFSNPPDWSKNVEYTFTGIYTFESLVKIIAR GFCIDGFTFLRDPWNWLDFSVIMMAYITEFVNLGNVSALRTFRVL RALKTISVIPGLKTIVGALIQSVKKLSDVMILTVFCLSVFALIGL QLFMGNLRNKCVVWPINFNESYLENGTKGFDWEEYINNKTNFYTV PGMLEPLLCGNSSDAGQCPEGYQCMKAGRNPNYGYTSFDTFSWAF LALFRLMTQDYWENLYQLTLRAAGKTYMIFFVLVIFVGSFYLVNL ILAVVAMAYEEQNQATLEEAEQKEAEFKAMLEQLKKQQEEAQAAA MATSAGTVSEDAIEEEGEEGGGSPRSSSEISKLSSKSAKERRNRR KKRKQKELSEGEEKGDPEKVFKSESEDGMRRKAFRLPDNRIGRKF SIMNQSLLSIPGSPFLSRHNSKSSIFSFRGPGRFRDPGSENEFAD DEHSTVEESEGRRDSLFIPIRARERRSSYSGYSGYSQGSRSSRIF PSLRRSVKRNSTVDCNGVVSLIGGPGSHIGGRLLPEATTEVEIKK KGPGSLLVSMDQLASYGRKDRINSIMSVVTNTLVEELEESQRKCP PCWYKFANTFLIWECHPYWIKLKEIVNLIVMDPFVDLAITICIVL NTLFMAMEHHPMTPQFEHVLAVGNLVFTGIFTAEMFLKLIAMDPY YYFQEGWNIFDGFIVSLSLMELSLADVEGLSVLRSFRLLRVFKLA KSWPTLNMLIKIIGNSVGALGNLTLVLAIIVFIFAVVGMQLFGKS YKECVCKINQDCELPRWHMHDFFHSFLIVFRVLCGEWIETMWDCM EVAGQAMCLIVFMMVMVIGNLVVLNLFLALLLSSFSADNLAATDD DGEMNNLQISVIRIKKGVAWTKLKVHAFMQAHFKQREADEVKPLD ELYEKKANCIANHTGADIHRNGDFQKNGNGTTSGIGSSVEKYIID EDHMSFINNPNLTVRVPIAVGESDFENLNTEDVSSESDPEGSKDK LDDTSSSEGSTIDIKPEVEEVPVEQPEEYLDPDACFTEGCVQRFK CCQVNIEEGLGKSWWILRKTCFLIVEHNWFETFIIFMILLSSGAL AFEDIYIEQRKTIRTILEYADKVFTYIFILEMLLKWTAYGFVKFF TNAWCWLDFLIVAVSLVSLIANALGYSELGAIKSLRTLRALRPLR ALSRFEGMRVVVNALVGAIPSIMNVLLVCLIFWLIFSIMGVNLFA GKYHYCFNETSEIRFEIEDVNNKTECEKLMEGNNTEIRWKNVKIN FDNVGAGYLALLQVATFKGWMDIMYAAVDSRKPDEQPKYEDNIYM YIYFVIFIIFGSFFTLNLFIGVIIDNFNQQKKKFGGQDIFMTEEQ KKYYNAMKKLGSKKPQKPIPRPLNKIQGIVFDFVTQQAFDIVIMM LICLNMVTMMVETDTQSKQMENILYWINLVFVIFFTCECVLKMFA LRHYYFTIGWNIFDFVVVILSIVGMFLADIIEKYFVSPTLFRVIR LARIGRILRLIKGAKGIRTLLFALMMSLPALFNIGLLLFLVMFIF SIFGMSNFAYVKHEAGIDDMFNFETFGNSMICLFQITTSAGWDGL LLPILNRPPDCSLDKEHPGSGFKGDCGNPSVGIFFFVSYIIISFL

		IVVNMYIAIILENFSVATEESADPLSEDDFETFYEIWEKFDPDAT QFIEYCKLADFADALEHPLRVPKPNTIELIAMDLPMVSGDRIHCL DILFAFTKRVLGDSGELDILRQQMEERFVASNPSKVSYEPITTTL RRKQEEVSAVVLQRAYRGHLARRGFICKKTTSNKLENGGTHREKK ESTPSTASLPSYDSVTKPEKEKQQRAEEGRRERAKRQKEVRESKC KVPVFTLEDFVGDWRQTAGYNLDQVLEQGGVSSLFQNLGVSVTPI QRIVLSGENGLKIDIHVIIPYEGLSGDQMGQIEKIFKVVYPVDDH HFKVILHYGTLVIDGVTPNMIDYFGRPYEGIAVFDGKKITVTGTL WNGNKIIDERLINPDGSLLFRVTINGVTGWRLCERILAGGGGSPS RLEEELRRRLTEP
SCN2A-nanoluc-alfa-tag-fusion	437	MAQSVLVPPGPDSFRFFTRESLAAIEQRIAEEKAKRPKQERKDED DENGPKPNSDLEAGKSLPFIYGDIPPEMVSVPLEDLDPYYINKKT FIVLNKGKAISRFSATPALYILTPFNPIRKLAIKILVHSLFNMLI MCTILTNCVFMTMSNPPDWTKNVEYTFTGIYTFESLIKILARGFC LEDFTFLRDPWNWLDFTVITFAYVTEFVDLGNVSALRTFRVLRAL KTISVIPGLKTIVGALIQSVKKLSDVMILTVFCLSVFALIGLQLF MGNLRNKCLQWPPDNSSFEINITSFFNNSLDGNGTTFNRTVSIFN WDEYIEDKSHFYFLEGQNDALLCGNSSDAGQCPEGYICVKAGRNP NYGYTSFDTFSWAFLSLFRLMTQDFWENLYQLTLRAAGKTYMIFF VLVIFLGSFYLINLILAVVAMAYEEQNQATLEEAEQKEAEFQQML EQLKKQQEEAQAAAAAASAESRDFSGAGGIGVFSESSSVASKLSS KSEKELKNRRKKKKQKEQSGEEEKNDRVRKSESEDSIRRKGFRFS LEGSRLTYEKRFSSPHQSLLSIRGSLFSPRRNSRASLFSFRGRAK DIGSENDFADDEHSTFEDNDSRRDSLFVPHRHGERRHSNVSQASR ASRVLPILPMNGKMHSAVDCNGVVSLVGGPSTLTSAGQLLPEGTT TETEIRKRRSSSYHVSMDLLEDPTSRQRAMSIASILTNTMEELEE SRQKCPPCWYKFANMCLIWDCCKPWLKVKHLVNLVVMDPFVDLAI TICIVLNTLFMAMEHYPMTEQFSSVLSVGNLVFTGIFTAEMFLKI IAMDPYYYFQEGWNIFDGFIVSLSLMELGLANVEGLSVLRSFRLL RVFKLAKSWPTLNMLIKIIGNSVGALGNLTLVLAIIVFIFAVVGM QLFGKSYKECVCKISNDCELPRWHMHDFFHSFLIVFRVLCGEWIE TMWDCMEVAGQTMCLTVFMMVMVIGNLVVLNLFLALLLSSFSSDN LAATDDDNEMNNLQIAVGRMQKGIDFVKRKIREFIQKAFVRKQKA LDEIKPLEDLNNKKDSCISNHTTIEIGKDLNYLKDGNGTTSGIGS SVEKYVVDESDYMSFINNPSLTVTVPIAVGESDFENLNTEEFSSE SDMEESKEKLNATSSSEGSTVDIGAPAEGEQPEVEPEESLEPEAC FTEDCVRKFKCCQISIEEGKGKLWWNLRKTCYKIVEHNWFETFIV FMILLSSGALAFEDIYIEQRKTIKTMLEYADKVFTYIFILEMLLK WVAYGFQVYFTNAWCWLDFLIVDVSLVSLTANALGYSELGAIKSL RTLRALRPLRALSRFEGMRVVVNALLGAIPSIMNVLLVCLIFWLI FSIMGVNLFAGKFYHCINYTTGEMFDVSVVNNYSECKALIESNQT ARWKNVKVNFDNVGLGYLSLLQVATFKGWMDIMYAAVDSRNVELQ PKYEDNLYMYLYFVIFIIFGSFFTLNLFIGVIIDNFNQQKKKFGG QDIFMTEEQKKYYNAMKKLGSKKPQKPIPRPANKFQGMVFDFVTK QVFDISIMILICLNMVTMMVETDDQSQEMTNILYWINLVFIVLFT GECVLKLISLRYYYFTIGWNIFDFVVVILSIVGMFLAELIEKYFV SPTLFRVIRLARIGRILRLIKGAKGIRTLLFALMMSLPALFNIGL LLFLVMFIYAIFGMSNFAYVKREVGIDDMFNFETFGNSMICLFQI TTSAGWDGLLAPILNSGPPDCDPDKDHPGSSVKGDCGNPSVGIFF FVSYIIISFLVVVNMYIAVILENFSVATEESAEPLSEDDFEMFYE VWEKFDPDATQFIEFAKLSDFADALDPPLLIAKPNKVQLIAMDLP

		MVSGDRIHCLDILFAFTKRVLGESGEMDALRIQMEERFMASNPSK VSYEPITTTLKRKQEEVSAIIIQRAYRRYLLKQKVKKVSSIYKKD KGKECDGTPIKEDTLIDKLNENSTPEKTDMTPSTTSPPSYDSVTK PEKEKFEKDKSEKEDKGKDIRESKKKVPVFTLEDFVGDWRQTAGY NLDQVLEQGGVSSLFQNLGVSVTPIQRIVLSGENGLKIDIHVIIP YEGLSGDQMGQIEKIFKVVYPVDDHHFKVILHYGTLVIDGVTPNM IDYFGRPYEGIAVFDGKKITVTGTLWNGNKIIDERLINPDGSLLF RVTINGVTGWRLCERILAGGGGSPSRLEEELRRRLTEP
Scn1a-nanoluc-alfa-tag-fusion	438	MEQTVLVPPGPDSFNFFTRESLAAIERRIAEEKAKNPKPDKKDDD ENGPKPNSDLEAGKNLPFIYGDIPPEMVSEPLEDLDPYYINKKTF IVLNKGKAIFRFSATSALYILTPFNPLRKIAIKILVHSLFSMLIM CTILTNCVFMTMSNPPDWTKNVEYTFTGIYTFESLIKIIARGFCL EDFTFLRDPWNWLDFTVITFAYVTEFVDLGNVSALRTFRVLRALK TISVIPGLKTIVGALIQSVKKLSDVMILTVFCLSVFALIGLQLFM GNLRNKCIQWPPTNASLEEHSIEKNITVNYNGTLINETVFEFDWK SYIQDSRYHYFLEGFLDALLCGNSSDAGQCPEGYMCVKAGRNPNY GYTSFDTFSWAFLSLFRLMTQDFWENLYQLTLRAAGKTYMIFFVL VIFLGSFYLINLILAVVAMAYEEQNQATLEEAEQKEAEFQQMIEQ LKKQQEAAQQAATATASEHSREPSAAGRLSDSSSEASKLSSKSAK ERRNRRKKRKQKEQSGGEEKDEDEFQKSESEDSIRRKGFRFSIEG NRLTYEKRYSSPHQSLLSIRGSLFSPRRNSRTSLFSFRGRAKDVG SENDFADDEHSTFEDNESRRDSLFVPRRHGERRNSNLSQTSRSSR MLAVFPANGKMHSTVDCNGVVSLVGGPSVPTSPVGQLLPEVIIDK PATDDNGTTTETEMRKRRSSSFHVSMDFLEDPSQRQRAMSIASIL TNTVEELEESRQKCPPCWYKFSNIFLIWDCSPYWLKVKHVVNLVV MDPFVDLAITICIVLNTLFMAMEHYPMTDHFNNVLTVGNLVFTGI FTAEMFLKIIAMDPYYYFQEGWNIFDGFIVTLSLVELGLANVEGL SVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLTLVLAII VFIFAVVGMQLFGKSYKDCVCKIASDCQLPRWHMNDFFHSFLIVF RVLCGEWIETMWDCMEVAGQAMCLTVFMMVMVIGNLVVLNLFLAL LLSSFSADNLAATDDDNEMNNLQIAVDRMHKGVAYVKRKIYEFIQ QSFIRKQKILDEIKPLDDLNNKKDSCMSNHTAEIGKDLDYLKDVN GTTSGIGTGSSVEKYIIDESDYMSFINNPSLTVTVPIAVGESDFE NLNTEDFSSESDLEESKEKLNESSSSSEGSTVDIGAPVEEQPVVE PEETLEPEACFTEGCVQRFKCCQINVEEGRGKQWWNLRRTCFRIV EHNWFETFIVFMILLSSGALAFEDIYIDQRKTIKTMLEYADKVFT YIFILEMLLKWVAYGYQTYFTNAWCWLDFLIVDVSLVSLTANALG YSELGAIKSLRTLRALRPLRALSRFEGMRVVVNALLGAIPSIMNV LLVCLIFWLIFSIMGVNLFAGKFYHCINTTTGDRFDIEDVNNHTD CLKLIERNETARWKNVKVNFDNVGFGYLSLLQVATFKGWMDIMYA AVDSRNVELQPKYEESLYMYLYFVIFIIFGSFFTLNLFIGVIIDN FNQQKKKFGGQDIFMTEEQKKYYNAMKKLGSKKPQKPIPRPGNKF QGMVFDFVTRQVFDISIMILICLNMVTMMVETDDQSEYVTTILSR INLVFIVLFTGECVLKLISLRHYYFTIGWNIFDFVVVILSIVGMF LAELIEKYFVSPTLFRVIRLARIGRILRLIKGAKGIRTLLFALMM SLPALFNIGLLLFLVMFIYAIFGMSNFAYVKREVGIDDMFNFETF GNSMICLFQITTSAGWDGLLAPILNSKPPDCDPNKVNPGSSVKGD CGNPSVGIFFFVSYIIISFLVVVNMYIAVILENFSVATEESAEPL SEDDFEMFYEVWEKFDPDATQFMEFEKLSQFAAALEPPLNLPQPN KLQLIAMDLPMVSGDRIHCLDILFAFTKRVLGESGEMDALRIQME ERFMASNPSKVSYQPITTTLKRKQEEVSAVIIQRAYRRHLLKRTV

		KQASFTYNKNKIKGGANLLIKEDMIIDRINENSITEKTDLTMSTA ACPPSYDRVTKPIVEKHEQEGKDEKAKGKKVPVFTLEDFVGDWRQ TAGYNLDQVLEQGGVSSLFQNLGVSVTPIQRIVLSGENGLKIDIH VIIPYEGLSGDQMGQIEKIFKVVYPVDDHHFKVILHYGTLVIDGV TPNMIDYFGRPYEGIAVFDGKKITVTGTLWNGNKIIDERLINPDG SLLFRVTINGVTGWRLCERILAGGGGSPSRLEEELRRRLTEP
Grin2b-nanoluc-alfa-tag-fusion	439	MKPRAECCSPKFWLVLAVLAVSGSRARSQKSPPSIGIAVILVGTS DEVAIKDAHEKDDFHHLSVVPRVELVAMNETDPKSIITRICDLMS DRKIQGVVFADDTDQEAIAQILDFISAQTLTPILGIHGGSSMIMA DKDESSMFFQFGPSIEQQASVMLNIMEEYDWYIFSIVTTYFPGYQ DFVNKIRSTIENSFVGWELEEVLLLDMSLDDGDSKIQNQLKKLQS PIILLYCTKEEATYIFEVANSVGLTGYGYTWIVPSLVAGDTDTVP AEFPTGLISVSYDEWDYGLPARVRDGIAIITTAASDMLSEHSFIP EPKSSCYNTHEKRIYQSNMLNRYLINVTFEGRNLSFSEDGYQMHP KLVIILLNKERKWERVGKWKDKSLQMKYYVWPRMCPETEEQEDDH LSIVTLEEAPFVIVESVDPLSGTCMRNTVPCQKRIVTENKTDEEP GYIKKCCKGFCIDILKKISKSVKFTYDLYLVTNGKHGKKINGTWN GMIGEVVMKRAYMAVGSLTINEERSEVVDFSVPFIETGISVMVSR SNGTVSPSAFLEPFSADVWVMMFVMLLIVSAVAVFVFEYFSPVGY NRCLADGREPGGPSFTIGKAIWLLWGLVFNNSVPVQNPKGTTSKI MVSVWAFFAVIFLASYTANLAAFMIQEEYVDQVSGLSDKKFQRPN DFSPPFRFGTVPNGSTERNIRNNYAEMHAYMGKFNQRGVDDALLS LKTGKLDAFIYDAAVLNYMAGRDEGCKLVTIGSGKVFASTGYGIA IQKDSGWKRQVDLAILQLFGDGEMEELEALWLTGICHNEKNEVMS SQLDIDNMAGVFYMLGAAMALSLITFICEHLFYWQFRHCFMGVCS GKPGMVFSISRGIYSCIHGVAIEERQSVMNSPTATMNNTHSNILR LLRTAKNMANLSGVNGSPQSALDFIRRESSVYDISEHRRSFTHSD CKSYNNPPCEENLFSDYISEVERTFGNLQLKDSNVYQDHYHHHHR PHSIGSASSIDGLYDCDNPPFTTQSRSISKKPLDIGLPSSKHSQL SDLYGKFSFKSDRYSGHDDLIRSDVSDISTHTVTYGNIEGNAAKR RKQQYKDSLKKRPASAKSRREFDEIELAYRRRPPRSPDHKRYFRD KEGLRDFYLDQFRTKENSPHWEHVDLTDIYKERSDDFKRDSVSGG GPCTNRSHIKHGTGDKHGVVSGVPAPWEKNLTNVEWEDRSGGNFC RSCPSKLHNYSTTVTGQNSGRQACIRCEACKKAGNLYDISEDNSL QELDQPAAPVAVTSNASTTKYPQSPTNSKAQKKNRNKLRRQHSYD TFVDLQKEEAALAPRSVSLKDKGRFMDGSPYAHMFEMSAGESTFA NNKSSVPTAGHHHHNNPGGGYMLSKSLYPDRVTQNPFIPTFGDDQ CLLHGSKSYFFRQPTVAGASKARPDFRALVTNKPVVSALHGAVPA RFQKDICIGNQSNPCVPNNKNPRAFNGSSNGHVYEKLSSIESDVK VPVFTLEDFVGDWRQTAGYNLDQVLEQGGVSSLFQNLGVSVTPIQ RIVLSGENGLKIDIHVIIPYEGLSGDQMGQIEKIFKVVYPVDDHH FKVILHYGTLVIDGVTPNMIDYFGRPYEGIAVFDGKKITVTGTLW NGNKIIDERLINPDGSLLFRVTINGVTGWRLCERILAGGGGSPSR LEEELRRRLTEP
SLC50A1-nanoluc-alfa-tag-fusion	440	MEAGGFLDSLIYGACVVFTLGMFSAGLSDLRHMRMTRSVDNVQFL PFLTTEVKKVPVFTLEDFVGDWRQTAGYNLDQVLEQGGVSSLFQN LGVSVTPIQRIVLSGENGLKIDIHVIIPYEGLSGDQMGQIEKIFK VVYPVDDHHFKVILHYGTLVIDGVTPNMIDYFGRPYEGIAVFDGK KITVTGTLWNGNKIIDERLINPDGSLLFRVTINGVTGWRLCERIL AGGGGSPSRLEEELRRRLTEP

TMEM258-nanoluc-alfa-tag-fusion	441	MELEAMSRYTSPVNPAVFPHLTVVLLAIGMFFTAWFFVYPFTEQP EDQHKVPVFTLEDFVGDWRQTAGYNLDQVLEQGGVSSLFQNLGVS VTPIQRIVLSGENGLKIDIHVIIPYEGLSGDQMGQIEKIFKVVYP VDDHHFKVILHYGTLVIDGVTPNMIDYFGRPYEGIAVFDGKKITV TGTLWNGNKIIDERLINPDGSLLFRVTINGVTGWRLCERILAGGG GSPSRLEEELRRRLTEP
FSHR-nanoluc-alfa-tag-fusion	442	MALLLVSLLAFLSLGSGCHHRICHCSNRVFLCQESKVTEIPSDLP RNAIELKVPVFTLEDFVGDWRQTAGYNLDQVLEQGGVSSLFQNLG VSVTPIQRIVLSGENGLKIDIHVIIPYEGLSGDQMGQIEKIFKVV YPVDDHHFKVILHYGTLVIDGVTPNMIDYFGRPYEGIAVFDGKKI TVTGTLWNGNKIIDERLINPDGSLLFRVTINGVTGWRLCERILAG GGGSPSRLEEELRRRLTEP
KCNQ1-nanoluc-alfa-tag-fusion	446	MAAASSPPRAERKRWGWGRLPGARRGSAGLAKKCPFSLELAEGGP AGGALYAPIAPGAPGPAPPASPAAPAAPPVASDLGPRPPVSLDPR VSIYSTRRPVLARTHVQGRVYNFLERPTGWKCFVYHFAVFLIVLV CLIFSVLSTIEQYAWRYYESSLEPYPDALATGTLFWMEIVLVVFF GTEYVVRLWSAGCRSKYVGLWGRLRFARKPISIIDLIVVVASMVV LCVGSKGQVFATSAIRGIRFLQILRMLHVDRQGGTWRLLGSVVFI HRQELITTLYIGFLGLIFSSYFVYLAEKDAVNESGRVEFGSYADA LWWGVVTVTTIGYGDKVPQTWVGKTIASCFSVFAISFFALPAGIL GSGFALKVQQKQRQKHFNRQIPAAASLIQTAWRCYAAENPDSSTW KIYIRKAPRSHTLLSPSPKPKKSVVVKKKKFKLDKDNGVTPGEKM LTVPHITCDPPEERRLDHFSVDGYDSSVRKSPTLLEVSMPHFMRT NSFAEDLDLEGETLLTPITHISQLREHHRATIKVIRRMQYFVAKK KFQQARKPYDVRDVIEQYSQGHLNLMVRIKELQRRLDQSIGKPSL FISVSEKSKDRGSNTIGARLNRVEDKVTQLDQRLALITDMLHQLL SLHGGSTPGSGGPPREGGAHITQPCGSGGSVDPELFLPSNTLPTY EQLTVPRRGPDEGSKVPVFTLEDFVGDWRQTAGYNLDQVLEQGGV SSLFQNLGVSVTPIQRIVLSGENGLKIDIHVIIPYEGLSGDQMGQ IEKIFKVVYPVDDHHFKVILHYGTLVIDGVTPNMIDYFGRPYEGI AVFDGKKITVTGTLWNGNKIIDERLINPDGSLLFRVTINGVTGWR LCERILAGGGGSPSRLEEELRRRLTEP

[00285] The amino acid sequence of exemplary fusion proteins comprising a control or a targeted engineered deubiquitinase are detailed in Table 8 below.

Table 8. Amino Acid Sequence of exemplary enDub Control and Screening Fusion Proteins

Description	SEQ ID NO	Amino Acid Sequence
FireflyLuciferase-P2A-nano (Control)	443	MEDAKNIKKGPAPFYPLEDGTAGEQLHKAMKRYALVPGTIAFTDA HIEVDITYAEYFEMSVRLAEAMKRYGLNTNHRIVVCSENSLQFFM PVLGALFIGVAVAPANDIYNERELLNSMGISQPTVVFVSKKGLQK ILNVQKKLPIIQKIIIMDSKTDYQGFQSMYTFVTSHLPPGFNEYD FVPESFDRDKTIALIMNSSGSTGLPKGVALPHRTACVRFSHARDP IFGNQIIPDTAILSVVPFHHGFGMFTTLGYLICGFRVVLMYRFEE ELFLRSLQDYKIQSALLVPTLFSFFAKSTLIDKYDLSNLHEIASG GAPLSKEVGEAVAKRFHLPGIRQGYGLTETTSAILITPEGDDKPG AVGKVVPFFEAKVVDLDTGKTLGVNQRGELCVRGPMIMSGYVNNP EATNALIDKDGWLHSGDIAYWDEDEHFFIVDRLKSLIKYKGYQVA PAELESILLQHPNIFDAGVAGLPDDDAGELPAAVVVLEHGKTMTE KEIVDYVASQVTTAKKLRGGVVFVDEVPKGLTGKLDARKIREILI

		KAKKGGKIAVTRLKGSGATNFSLLKQAGDVEENPGPRSGTGSSGE VQLQESGGGLVQPGGSLRLSCTASGVTISALNAMAMGWYRQAPGE RRVMVAAVSERGNAMYRESVQGRFTVTRDFTNKMVSLQMDNLKPE DTAVYYCHVLEDRVDSFHDYWGQGTQVTVSS
FireflyLuciferase-P2A-Cezanne (Control)	444	MEDAKNIKKGPAPFYPLEDGTAGEQLHKAMKRYALVPGTIAFTDA HIEVDITYAEYFEMSVRLAEAMKRYGLNTNHRIVVCSENSLQFFM PVLGALFIGVAVAPANDIYNERELLNSMGISQPTVVFVSKKGLQK ILNVQKKLPIIQKIIIMDSKTDYQGFQSMYTFVTSHLPPGFNEYD FVPESFDRDKTIALIMNSSGSTGLPKGVALPHRTACVRFSHARDP IFGNQIIPDTAILSVVPFHHGFGMFTTLGYLICGFRVVLMYRFEE ELFLRSLQDYKIQSALLVPTLFSFFAKSTLIDKYDLSNLHEIASG GAPLSKEVGEAVAKRFHLPGIRQGYGLTETTSAILITPEGDDKPG AVGKVVPFFEAKVVDLDTGKTLGVNQRGELCVRGPMIMSGYVNNP EATNALIDKDGWLHSGDIAYWDEDEHFFIVDRLKSLIKYKGYQVA PAELESILLQHPNIFDAGVAGLPDDDAGELPAAVVVLEHGKTMTE KEIVDYVASQVTTAKKLRGGVVFVDEVPKGLTGKLDARKIREILI KAKKGGKIAVTRLKGSGATNFSLLKQAGDVEENPGPRSGTGSPPS FSEGSGGSRTPEKGFSDREPTRPPRPILQRQDDIVQEKRLSRGIS HASSSIVSLARSHVSSNGGGGGSNEHPLEMPICAFQLPDLTVYNE DFRSFIERDLIEQSMLVALEQAGRLNWWVSVDPTSQRLLPLATTG DGNCLLHAASLGMWGFHDRDLMLRKALYALMEKGVEKEALKRRWR WQQTQQNKESGLVYTEDEWQKEWNELIKLASSEPRMHLGTNGANC GGVESSEEPVYESLEEFHVFVLAHVLRRPIVVVADTMLRDSGGEA FAPIPFGGIYLPLEVPASQCHRSPLVLAYDQAHFSALVSMEQKEN TKEQAVIPLTDSEYKLLPLHFAVDPGKGWEWGKDDSDNVRLASVI LSLEVKLHLLHSYMNVKWIPLSSDAQAPLAQ
FireflyLuciferase-P2A-a_alfatag_nano-Cezanne	445	MEDAKNIKKGPAPFYPLEDGTAGEQLHKAMKRYALVPGTIAFTDA HIEVDITYAEYFEMSVRLAEAMKRYGLNTNHRIVVCSENSLQFFM PVLGALFIGVAVAPANDIYNERELLNSMGISQPTVVFVSKKGLQK ILNVQKKLPIIQKIIIMDSKTDYQGFQSMYTFVTSHLPPGFNEYD FVPESFDRDKTIALIMNSSGSTGLPKGVALPHRTACVRFSHARDP IFGNQIIPDTAILSVVPFHHGFGMFTTLGYLICGFRVVLMYRFEE ELFLRSLQDYKIQSALLVPTLFSFFAKSTLIDKYDLSNLHEIASG GAPLSKEVGEAVAKRFHLPGIRQGYGLTETTSAILITPEGDDKPG AVGKVVPFFEAKVVDLDTGKTLGVNQRGELCVRGPMIMSGYVNNP EATNALIDKDGWLHSGDIAYWDEDEHFFIVDRLKSLIKYKGYQVA PAELESILLQHPNIFDAGVAGLPDDDAGELPAAVVVLEHGKTMTE KEIVDYVASQVTTAKKLRGGVVFVDEVPKGLTGKLDARKIREILI KAKKGGKIAVTRLKGSGATNFSLLKQAGDVEENPGPRSGTGSSGE VQLQESGGGLVQPGGSLRLSCTASGVTISALNAMAMGWYRQAPGE RRVMVAAVSERGNAMYRESVQGRFTVTRDFTNKMVSLQMDNLKPE DTAVYYCHVLEDRVDSFHDYWGQGTQVTVSSGAPGSGPPSFSEGS GGSRTPEKGFSDREPTRPPRPILQRQDDIVQEKRLSRGISHASSS IVSLARSHVSSNGGGGGSNEHPLEMPICAFQLPDLTVYNEDFRSF IERDLIEQSMLVALEQAGRLNWWVSVDPTSQRLLPLATTGDGNCL LHAASLGMWGFHDRDLMLRKALYALMEKGVEKEALKRRWRWQQTQ QNKESGLVYTEDEWQKEWNELIKLASSEPRMHLGTNGANCGGVES SEEPVYESLEEFHVFVLAHVLRRPIVVVADTMLRDSGGEAFAPIP FGGIYLPLEVPASQCHRSPLVLAYDQAHFSALVSMEQKENTKEQA

		VIPLTDSEYKLLPLHFAVDPGKGWEWGKDDSDNVRLASVILSLEV KLHLLHSYMNVKWIPLSSDAQAPLAQ

[00286] The assay was conducted with utilizing the tagged proteins and targeted enDubs described above in Tables 7 and 8. The results of the KCNQ1 targeting are shown in **FIG. 3**, showing a 3.8-fold increase in KCNQ1 protein expression. The results of the SCN1A targeting are shown in **FIG. 4**, showing a 4.4-fold increase in SCN1A protein expression. The results of the GRIN2B targeting are shown in **FIG. 5**, showing a 5.3-fold increase in GRIN2B protein expression. The results of the SLC50A1 targeting are shown in **FIG. 6**, showing a 2.03-fold increase in SLC50A1 protein expression. The results of the TREM258 targeting are shown in **FIG. 7**, showing a 2.77-fold increase in TREM258 protein expression. The results of the FSHR targeting are shown in **FIG. 8**, showing a 1.33-fold increase in FSHR protein expression. The control used for the SLC50A1, TREM258, and FSHR experiments is the engineered deubiquitinase without the nanobody targeting the alfa-tag. Normalization of transduction efficiency was performed using the firefly luciferase signal as the reference and the ratio between NLuc signal divided by firefly luciferase signal plotted on the y axes.

* * *

[00287] The invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications are intended to fall within the scope of the appended claims.

[00288] All references (e.g., publications or patents or patent applications) cited herein are incorporated herein by reference in their entireties and for all purposes to the same extent as if each individual reference (e.g., publication or patent or patent application) was specifically and individually indicated to be incorporated by reference in its entirety for all purposes. Other embodiments are within the following claims.

CLAIMS

What is claimed is:

1. A fusion protein comprising:
    a. an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof; and
    b. a targeting domain comprising a targeting moiety that specifically binds a membrane protein that is not an ion channel.

2. The fusion protein of claim 1, wherein said deubiquitinase is a cysteine protease or a metalloprotease.

3. The fusion protein of claim 2, wherein said deubiquitinase is a cysteine protease.

4. The fusion protein of claim 3, wherein said cysteine protease is a ubiquitin-specific protease (USP), a ubiquitin C-terminal hydrolase (UCH), a Machado-Josephin domain protease (MJD), an ovarian tumour protease (OTU), a MINDY protease, or a ZUFSP protease.

5. The fusion protein of claim 4, wherein said cysteine protease is a USP.

6. The fusion protein of claim 5, wherein said USP is USP1, USP2, USP3, USP4, USP5, USP6, USP7, USP8, USP9X, USP9Y, USP10, USP11, USP12, USP13, USP14, USP15, USP16, USP17, USP17L2, USP17L3, USP17L4, USP17L5, USP17L7, USP17L8, USP18, USP19, USP20, USP21, USP22, USP23, USP24, USP25, USP26, USP27X, USP28, USP29, USP30, USP31, USP32, USP33, USP34, USP35, USP36, USP37, USP38, USP39, USP40, USP41, USP42, USP43, USP44, USP45, or USP46.

7. The fusion protein of claim 4, wherein said cysteine protease is a UCH.

8. The fusion protein of claim 7, wherein said UCH is BAP1, UCHL1, UCHL3, or UCHL5.

9. The fusion protein of claim 4, wherein said cysteine protease is a MJD.

10. The fusion protein of claim 9, wherein said MJD is ATXN3 or ATXN3L.

11. The fusion protein of claim 4, wherein said cysteine protease is a OTU.

12. The fusion protein of claim 11, wherein said OTU is OTUB1 or OTUB2.

13. The fusion protein of claim 4, wherein said cysteine protease is a MINDY.

14. The fusion protein of claim 13, wherein said MINDY is MINDY1, MINDY2, MINDY3, or MINDY4.

15. The fusion protein of claim 4, wherein said cysteine protease is a ZUFSP.

16. The fusion protein of claim 15, wherein said ZUFSP is ZUP1.

17. The fusion protein of claim 2, wherein said deubiquitinase is a metalloprotease.

18. The fusion protein of claim 17, wherein said metalloprotease is a Jab1/Mov34/Mpr1 Pad1 N-terminal+ (MPN+) (JAMM) domain protease.

19. The fusion protein of any one of the preceding claims, wherein said deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 1-112.

20. The fusion protein of any one of the preceding claims, wherein said catalytic domain comprises a catalytic domain derived from a deubiquitinase at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 1-112.

21. The fusion protein of any one of the preceding claims, wherein said catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 113-220 or 293.

22. The fusion protein of any one of the preceding claims, wherein said catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 293.

23. The fusion protein of any one of the preceding claims, wherein said moiety that specifically binds a membrane protein comprises an antibody, or functional fragment or functional variant thereof.

24. The fusion protein of claim 23, wherein said antibody, or functional fragment or functional variant thereof, comprises a full-length antibody, a single chain variable fragment (scFv), a scFv2, a scFv-Fc, a Fab, a Fab', a F(ab')2, a F(v), a VHH, or a $(VHH)_2$.

25. The fusion protein of claim 23, wherein said antibody, or functional fragment or functional variant thereof, comprises a VHH or a $(VHH)_2$.

26. The fusion protein of any one of the preceding claims, wherein the membrane protein is selected from the group consisting of solute carrier family 2, facilitated glucose transporter member 1 (SLC2A1), proline-rich transmembrane protein 2 (PRRT2), usherin (USH2A), protocadherin-19 (PCDH19), tuberin (TSC2), hamartin (TSC1), dystrophin (DMD), Rhodopsin

(RHO), protein jagged-1 (JAG1), inositol 1,4,5-trisphosphate receptor type 1 (ITPR1), sugar transporter SWEET1 (SLC50A1), transmembrane protein 258 (TMEM258), or follicle stimulating hormone receptor (FSHR).

27. The fusion protein of any one of the preceding claims, wherein the membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 221-227 or 243-245.

28. The fusion protein of any one of the preceding claims, wherein said effector domain is directly operably connected to said targeting domain.

29. The fusion protein of any one of claims 1-28, wherein said effector domain is indirectly operably connected to said targeting domain.

30. The fusion protein of claim 28, wherein said effector domain is indirectly operably connected to said targeting domain via a peptide linker.

31. The fusion protein of claim 29, wherein said effector domain is indirectly operably connected to said targeting domain via a peptide linker of sufficient length such that said effector domain and said targeting domain can simultaneous bind the respective target proteins.

32. The fusion protein of claim 30 or 31, wherein said peptide linker comprises the amino acid sequence of any one of SEQ ID NOS: 297-424, or the amino acid sequence of any one of SEQ ID NOS: 297-424 comprising 1, 2, or 3 amino acid modifications.

33. The fusion protein of claim 32, wherein said peptide linker comprises the amino acid sequence of any one of SEQ ID NOS: 297-306, or the amino acid sequence of any one of SEQ ID NOS: 297-306 comprising 1, 2, or 3 amino acid modifications.

34. The fusion protein of any one of the preceding claims, wherein said effector domain is operably connected either directly or indirectly to the C terminus of said targeting domain.

35. The fusion protein of any one of claims 1-33, wherein said effector moiety is operably connected either directly or indirectly to the N terminus of said targeting domain.

36. A fusion protein comprising:

a. an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof; and

b. a targeting domain comprising a targeting moiety that specifically binds a membrane protein selected from the group consisting of glutamate receptor

ionotropic NMDA 2B (GRIN2B), cystic fibrosis transmembrane conductance regulator (CFTR), sodium channel protein type 1 subunit alpha (SCN1A), copper-transporting ATPase 2 (ATP7B), potassium voltage-gated channel subfamily KQT member 2 (KCNQ2), sodium channel protein type 2 subunit alpha (SCN2A), voltage-dependent P/Q-type calcium channel subunit alpha-1A (CACNA1A), sodium channel protein type 8 subunit alpha (SCN8A), glutamate receptor ionotropic, NMDA 2A (GRIN2A), sodium- and chloride-dependent GABA transporter 1 (SLC6A1), sodium/potassium-transporting ATPase subunit alpha-2 (ATP1A2), sodium/potassium-transporting ATPase subunit alpha-3 (ATP1A3), sodium channel protein type 9 subunit alpha (SCN9A), gamma-aminobutyric acid receptor subunit beta-3 (GABRB3), and potassium voltage-gated channel subfamily KQT member 3 (KCNQ3).

37. The fusion protein of claim 36, wherein said moiety that specifically binds a membrane protein comprises an antibody, or functional fragment or functional variant thereof.

38. The fusion protein of claim 37, wherein said antibody, or functional fragment or functional variant thereof, comprises a full-length antibody, a single chain variable fragment (scFv), a scFv2, a scFv-Fc, a Fab, a Fab', a F(ab')2, a F(v), a VHH, or a $(VHH)_2$.

39. The fusion protein of claim 38, wherein said antibody, or functional fragment or functional variant thereof, comprises a VHH or a $(VHH)_2$.

40. The fusion protein of any one of claims 36-39, wherein the membrane protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 228-245.

41. The fusion protein of any one of claims 36-40, wherein said deubiquitinase is a cysteine protease or a metalloprotease.

42. The fusion protein of claim 41, wherein said deubiquitinase is a cysteine protease.

43. The fusion protein of claim 41, wherein said cysteine protease is a ubiquitin-specific protease (USP), a ubiquitin C-terminal hydrolase (UCH), a Machado-Josephin domain protease (MJD), an ovarian tumour protease (OTU), a MINDY protease, or a ZUFSP protease.

44. The fusion protein of claim 43, wherein said cysteine protease is a USP.

45. The fusion protein of claim 44, wherein said USP is USP1, USP2, USP3, USP4, USP5, USP6, USP7, USP8, USP9X, USP9Y, USP10, USP11, USP12, USP13, USP14, USP15, USP16,

USP17, USP17L2, USP17L3, USP17L4, USP17L5, USP17L7, USP17L8, USP18, USP19, USP20, USP21, USP22, USP23, USP24, USP25, USP26, USP27X, USP28, USP29, USP30, USP31, USP32, USP33, USP34, USP35, USP36, USP37, USP38, USP39, USP40, USP41, USP42, USP43, USP44, USP45, or USP46.

46. The fusion protein of claim 43, wherein said cysteine protease is a UCH.

47. The fusion protein of claim 46, wherein said UCH is BAP1, UCHL1, UCHL3, or UCHL5.

48. The fusion protein of claim 43, wherein said cysteine protease is a MJD.

49. The fusion protein of claim 48, wherein said MJD is ATXN3 or ATXN3L.

50. The fusion protein of claim 43, wherein said cysteine protease is a OTU.

51. The fusion protein of claim 50, wherein said OTU is OTUB1 or OTUB2.

52. The fusion protein of claim 43, wherein said cysteine protease is a MINDY.

53. The fusion protein of claim 52, wherein said MINDY is MINDY1, MINDY2, MINDY3, or MINDY4.

54. The fusion protein of claim 43, wherein said cysteine protease is a ZUFSP.

55. The fusion protein of claim 54, wherein said ZUFSP is ZUP1.

56. The fusion protein of claim 41, wherein said deubiquitinase is a metalloprotease.

57. The fusion protein of claim 56, wherein said metalloprotease is a Jab1/Mov34/Mpr1 Pad1 N-terminal+ (MPN+) (JAMM) domain protease.

58. The fusion protein of any one of claims 36-57, wherein said deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 1-112.

59. The fusion protein of any one of claims 36-58, wherein said catalytic domain comprises a catalytic domain derived from a deubiquitinase at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 1-112.

60. The fusion protein of any one of claims 36-59, wherein said catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS: 113-220 or 293.

61. The fusion protein of any one of claims 36-60, wherein said catalytic domain comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 293.

62. The fusion protein of any one of claims 36-61, wherein said effector domain is directly operably connected to said targeting domain.

63. The fusion protein of any one of claims 36-62, wherein said effector domain is indirectly operably connected to said targeting domain.

64. The fusion protein of claim 63, wherein said effector domain is indirectly operably connected to said targeting domain via a peptide linker.

65. The fusion protein of claim 64, wherein said effector domain is indirectly operably connected to said targeting domain via a peptide linker of sufficient length such that said effector domain and said targeting domain can simultaneous bind the respective target proteins.

66. The fusion protein of claim 64 or 65, wherein said peptide linker comprises the amino acid sequence of any one of SEQ ID NOS: 297-424, or the amino acid sequence of any one of SEQ ID NOS: 297-424 comprising 1, 2, or 3 amino acid modifications.

67. The fusion protein of claim 66, wherein said peptide linker comprises the amino acid sequence of any one of SEQ ID NOS: 297-306, or the amino acid sequence of any one of SEQ ID NOS: 297-306 comprising 1, 2, or 3 amino acid modifications.

68. The fusion protein of any one of claims 36-67, wherein said effector domain is operably connected either directly or indirectly to the C terminus of said targeting domain.

69. The fusion protein of any one of claims 36-68, wherein said effector moiety is operably connected either directly or indirectly to the N terminus of said targeting domain.

70. A nucleic acid molecule encoding the fusion protein of any one of claims 1-69.

71. The nucleic acid molecule of claim 70, wherein the nucleic acid molecule is a DNA molecule.

72. The nucleic acid molecule of claim 70, wherein the nucleic acid molecule is an RNA molecule.

73. A vector comprising the nucleic acid molecule of any one of claims 70-72.

74. The vector of claim 73, wherein the vector is a plasmid or a viral vector.

75. A viral particle comprising the nucleic acid of any one of claims 70-72.

76. An in vitro cell or population of cells comprising the fusion protein of any one of claims 1-69, the nucleic acid molecule of any one of claims 70-72, or the vector of any one of claims 73-74.

77. A pharmaceutical composition comprising the fusion protein of any one of claims 1-69, the nucleic acid molecule of any one of claims 70-72, the vector of any one of claims 73-74, or the viral particle of claim 75, and an excipient.

78. A method of making the fusion protein of any one of claims 1-69, comprising

a. introducing into an in vitro cell or population of cells the nucleic acid molecule of any one of claims 70-72, the vector of any one of claims 73-74, the viral particle of claim 75;

b. culturing the cell or population of cells in a culture medium under conditions suitable for expression of the fusion protein,

c. isolating the fusion protein from the culture medium, and

d. optionally purifying the fusion protein.

79. A method of treating or preventing a disease in a subject comprising administering the fusion protein of any one of claims 1-69, the nucleic acid of any one of claims 70-72, the vector of any one of claims 73-74, the viral particle of claim 75, or the pharmaceutical composition of claim 77, to a subject in need thereof.

80. The method of claim 79, wherein the subject is human.

81. The method of any one of claims 79-80, wherein the disease is associated with decreased expression of a functional version of the membrane protein relative to a non-diseased control.

82. The method of any one of claims 79-81, wherein the disease is associated with decreased stability of a functional version of the membrane protein relative to a non-diseased control.

83. The method of any one of claims 79-82, wherein the disease is associated with increased ubiquitination and degradation of the membrane protein relative to a non-diseased control.

84. The method of any one of claims 79-83, wherein the disease is a genetic disease.

85. The method of claim 84, wherein the genetic disease is a haploinsufficiency disease.

86. The method of any one of claims 79-85, wherein the disease is a GRIN2B-Related Disorder, a SCN2A-Related Disorder, a SCN8A-Related Disorder, SLC6A1-Related Disorder, a PRRT2 Dyskinesia & Epilepsy, a GRIN2A-Related Disorder, a CACNA1A-Related Disorder, a SCN9A Epilepsy, a PCDH19 Encephalopathy, GLUT1 deficiency syndrome, episodic kinesigenic

dyskinesia 1, Usher syndrome type 2A, early infantile epileptic encephalopathy type 9, tuberous sclerosis type 2; tuberous sclerosis type 1, a KCNQ2-Related Disorder (e.g., epileptic encephalopathy), Becker Muscular Dystrophy, autosomal Dominant RP, or Alagille syndrome 1, Gillespie Syndrome.

87. The method of any one of claims 79-86, wherein the disease is early infantile epileptic encephalopathy type 11, early infantile epileptic encephalopathy type 13, early infantile epileptic encephalopathy type 27, cystic fibrosis, Dravet syndrome, Wilson disease, episodic ataxia type 2; epilepsy (e.g., focal, with speech disorder and with or without mental retardation), myoclonic-atonic epilepsy, alternating hemiplegia of childhood, alternating hemiplegia of childhood type 2, epilepsy type 7, GABRB3 associated epilepsy, or a KCNQ2-Related Disorder (e.g., epileptic encephalopathy).

88. The method of any one of claims 79-87, wherein the disease is a GRIN2B-Related Disorder, a SCN2A-Related Disorder, a SCN8A-Related Disorder, SLC6A1-Related Disorder, a PRRT2 Dyskinesia & Epilepsy, a GRIN2A-Related Disorder, a CACNA1A-Related Disorder, a SCN9A Epilepsy, a PCDH19 Encephalopathy, early infantile epileptic encephalopathy type 9, early infantile epileptic encephalopathy type 11, early infantile epileptic encephalopathy type 13, early infantile epileptic encephalopathy type 27, cystic fibrosis, Dravet syndrome, Wilson disease, episodic ataxia type 2; GLUT1 deficiency syndrome, episodic kinesigenic dyskinesia 1, epilepsy (e.g., focal, with speech disorder and with or without mental retardation), KCNQ2 encephalopathy, myoclonic-atonic epilepsy, Usher syndrome type 2A, alternating hemiplegia of childhood, alternating hemiplegia of childhood type 2, epilepsy type 7, GABRB3 associated epilepsy; tuberous sclerosis type 2; tuberous sclerosis type 1, Becker Muscular Dystrophy, autosomal Dominant RP, Alagille syndrome 1, or Gillespie Syndrome.

89. Said method of any one of claims 79-88, wherein

a. said target membrane protein is GRIN2B, and said disease is a GRIN2B related disorder (e.g., an epileptic encephalopathy);

b. said target membrane protein is GRIN2B, and said disease is an early infantile epileptic encephalopathy;

c. said target membrane protein is GRIN2B, and said disease is early infantile epileptic encephalopathy type 27;

d. said target membrane protein is CFTR, and said disease is cystic fibrosis;

e. said target membrane protein is SCN1A, and said disease is Dravet syndrome;

f. said target membrane protein is ATP7B, and said disease is Wilson disease;

g. said target membrane protein is CACNA1A, and said disease is a CACA1A related disorder;

h. said target membrane protein is CACNA1A, and said disease is episodic ataxia type 2;

i. said target membrane protein is KCNQ2, and said disease is an KCNQ2 encephalopathy;

j. said target membrane protein is KCNQ2, and said disease is an epileptic encephalopathy;

k. said target membrane protein is SCN2A, and said disease is a SCN2A related disorder (e.g., an epileptic encephalopathy);

l. said target membrane protein is SCN2A, and said disease is early infantile epileptic encephalopathy type 11;

m. said target membrane protein is SLC2A1, and said disease is GLUT1 deficiency syndrome;

n. said target membrane protein is SCN8A, and said disease is a SCN8A related disorder (e.g., an epileptic encephalopathy);

o. said target membrane protein is SCN8A, and said disease is an epileptic encephalopathy;

p. said target membrane protein is SCN8A, and said disease is early infantile epileptic encephalopathy type 13;

q. said target membrane protein is PRRT2, and said disease is a PRRPT2 dyskinesia and/or epilepsy;

r. said target membrane protein is PRRT2, and said disease is an episodic kinesigenic dyskinesia type;

s. said target membrane protein is PRRT2, and said disease is episodic kinesigenic dyskinesia type 1;

t. said target membrane protein is GRIN2A, and said disease is a GRIN2A related disorder;

u. said target membrane protein is GRIN2A, and said disease is epilepsy;

v. said target membrane protein is GRIN2A, and said disease is focal epilepsy;

w. said target membrane protein is GRIN2A, and said disease is focal epilepsy with speech disorder and with or without mental retardation;

x. said target membrane protein is SLC6A1, and said disease is a SLC6A1 related disorder;

y. said target membrane protein is SLC6A1, and said disease is epilepsy;

z. said target membrane protein is SLC6A1, and said disease is myoclonic-atonic epilepsy;

aa. said target membrane protein is USH2A, and said disease is Usher syndrome;

bb. said target membrane protein is USH2A, and said disease is Usher syndrome type 2A;

cc. said target membrane protein is ATP1A2, and said disease is alternating hemiplegia of childhood;

dd. said target membrane protein is ATP1A2, and said disease is alternating hemiplegia of childhood type 1;

ee. said target membrane protein is ATP1A3, and said disease is alternating hemiplegia of childhood;

ff. said target membrane protein is ATP1A3, and said disease is alternating hemiplegia of childhood type 2;

gg. said target membrane protein is SCN9A, and said disease an SCN9A epilepsy;

hh. said target membrane protein is SCN9A1, and said disease an SCN9A epilepsy;

ii. said target membrane protein is SCN9A1, and said disease is epilepsy;

jj. said target membrane protein is SCN9A1, and said disease is epilepsy type 7;

kk. said target membrane protein is PCDH19, and said disease is PCDH19 encephalopathy;

ll. said target membrane protein is PCDH19, and said disease is an early infantile epileptic encephalopathy;

mm. said target membrane protein is PCDH19, and said disease is early infantile epileptic encephalopathy type 9;

nn. said target membrane protein is GABRB3, and said disease is epilepsy;

oo. said target membrane protein is GABRB3, and said disease is GABRB3 associated epilepsy;

pp. said target membrane protein is TSC2, and said disease is tuberous sclerosis;

qq. said target membrane protein is TSC2, and said disease is tuberous sclerosis type 2;

rr. said target membrane protein is TSC2, and said disease is tuberous sclerosis type 1;

ss. said target membrane protein is TSC1, and said disease is tuberous sclerosis;

tt. said target membrane protein is TSC1, and said disease is tuberous sclerosis type 1;

uu. said target membrane protein is TSC1, and said disease is tuberous sclerosis type 2;

vv. said target membrane protein is KCNQ3, and said disease is KCNQ2-Related Disorders (Epileptic Encephalopathy);

ww. said target membrane protein is DMD, and said disease is Becker Muscular Dystrophy;

xx. said target membrane protein is RHO, and said disease is Autosomal Dominant RP;

yy. said target membrane protein is JAG1, and said disease is Alagille syndrome 1;

zz. said target membrane protein is ITPR1, and said disease is Gillespie Syndrome; or

aaa. said target membrane protein is FSHR, and said disease is ovarian dysgenesis 1 (ODG1).

90. The method of any one of claims 79-89, wherein the fusion protein is administered at a therapeutically effective dose.

91. The method of any one of claims 79-90, wherein the fusion protein is administered systematically or locally.

92. The method of any one of claims 79-91, wherein the fusion protein is administered intravenously, subcutaneously, or intramuscularly.

93. The fusion protein of any one of claims 1-69, the polynucleotide of claim 70, the DNA of claim 71, the RNA of claim 72, the vector of any one of claims 73-74, the viral particle of claim 75, or the pharmaceutical composition of claim 77 for use as a medicament.

94. The fusion protein of any one of claims 1-69, the polynucleotide of claim 70, the DNA of claim 71, the RNA of claim 72, the vector of any one of claims 73-74, the viral particle of claim 75, or the pharmaceutical composition of claim 77 for use in treating or inhibiting a genetic disorder.



FIG. 1A

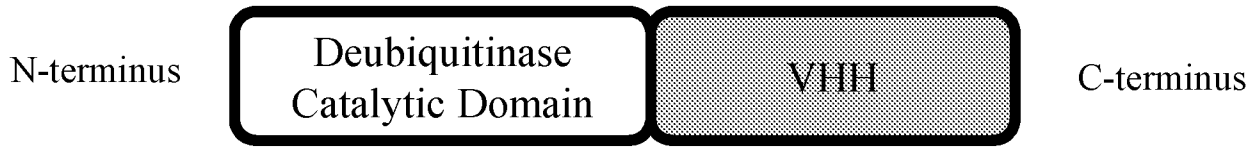


FIG. 1B

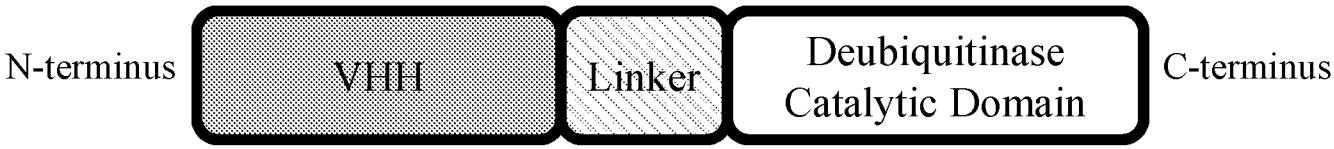


FIG. 1C

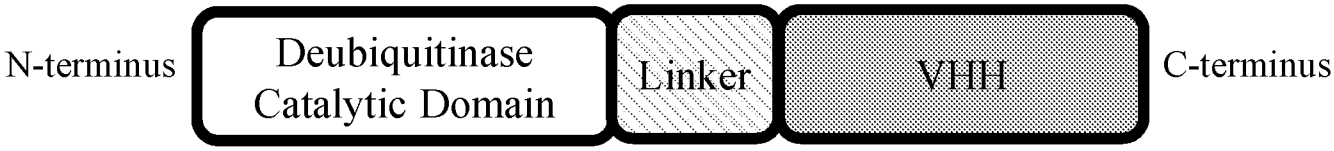


FIG. 1D

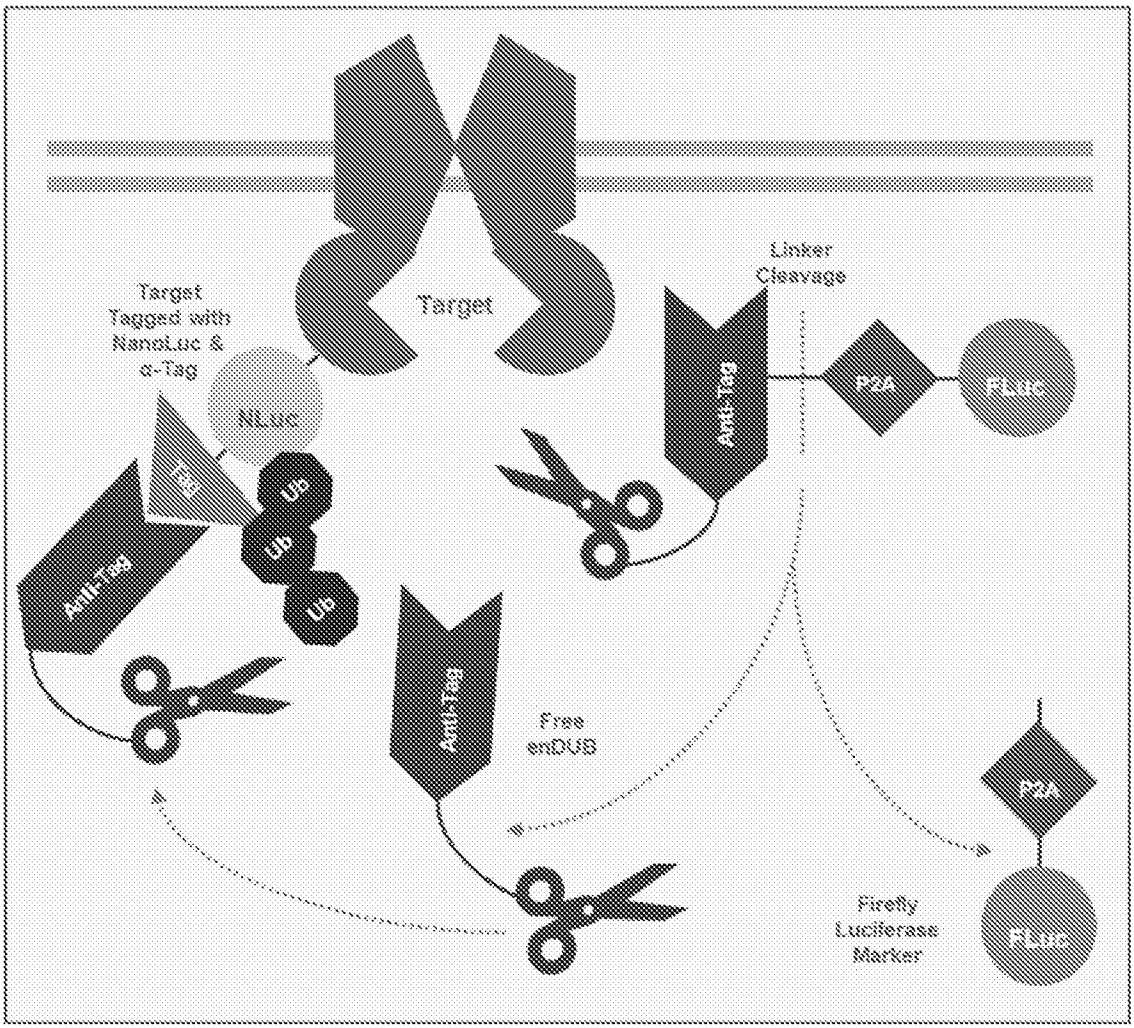

Target
Target Tagged with NanoLuc & α-Tag
NLuc
α-Tag
Ub
Ub
Ub
Anti-Tag
Anti-Tag
Linker Cleavage
Anti-Tag
P2A
FLuc
Free enDUB
P2A
Firefly Luciferase Marker
FLuc

FIG. 2

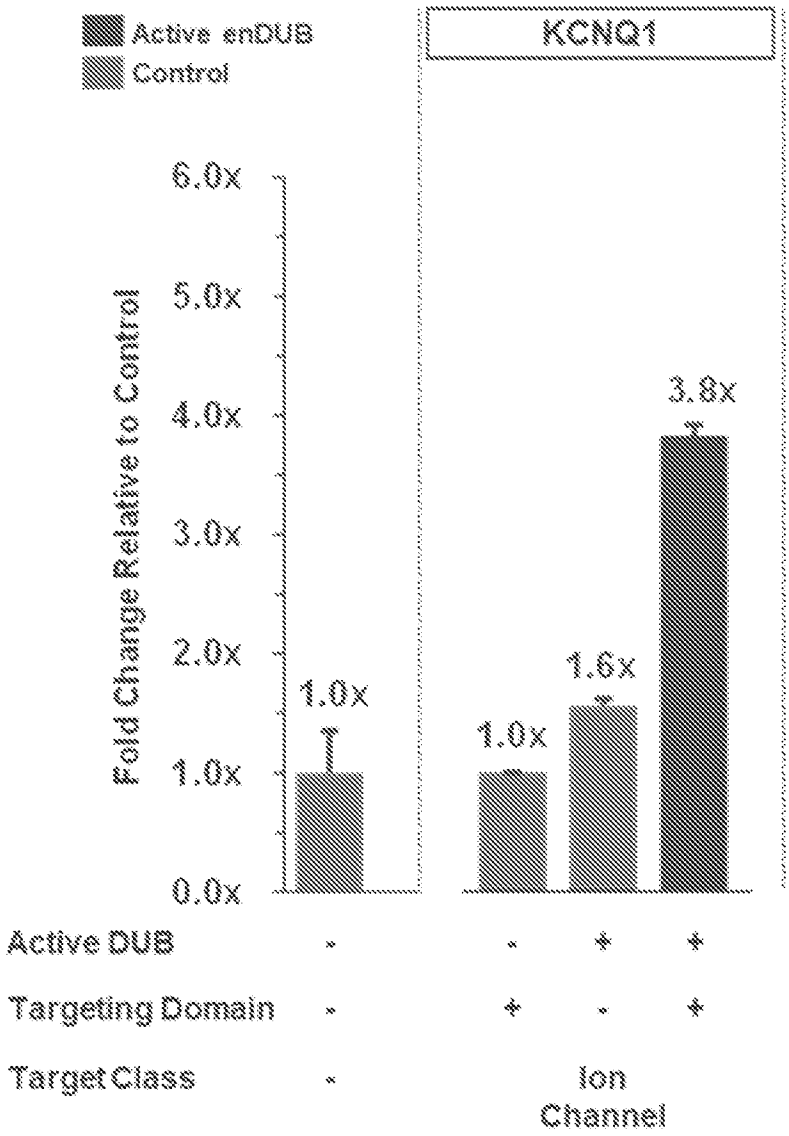

Active enDUB
Control
KCNQ1
Fold Change Relative to Control
6.0x
5.0x
4.0x
3.0x
2.0x
1.0x
0.0x
1.0x
1.0x
1.6x
3.8x
Active DUB
Targeting Domain
Target Class
Ion Channel

FIG. 3

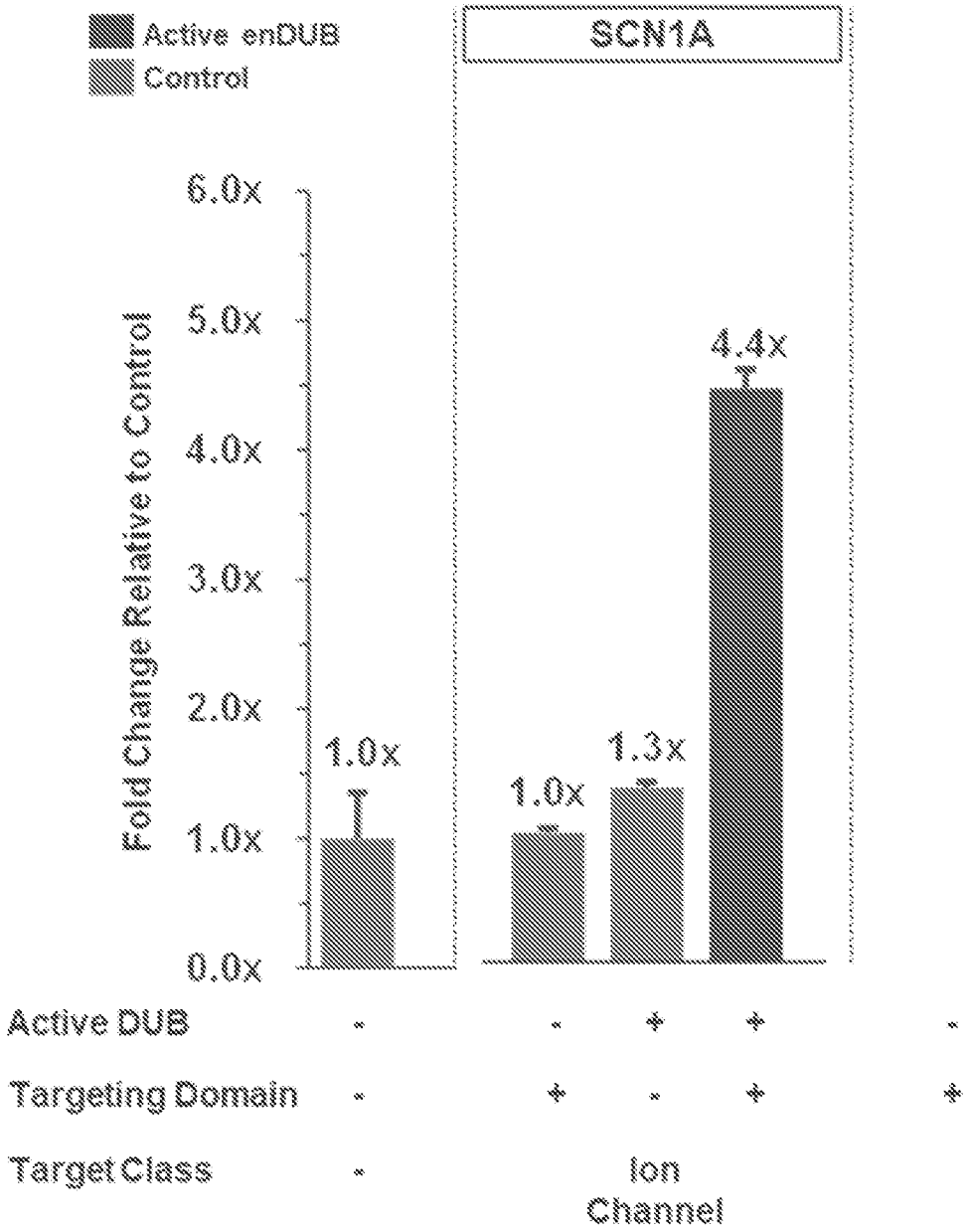

Active enDUB
Control
SCN1A
Fold Change Relative to Control
6.0x
5.0x
4.0x
3.0x
2.0x
1.0x
0.0x
1.0x
1.0x
1.3x
4.4x
Active DUB
Targeting Domain
Target Class
Ion Channel

FIG. 4

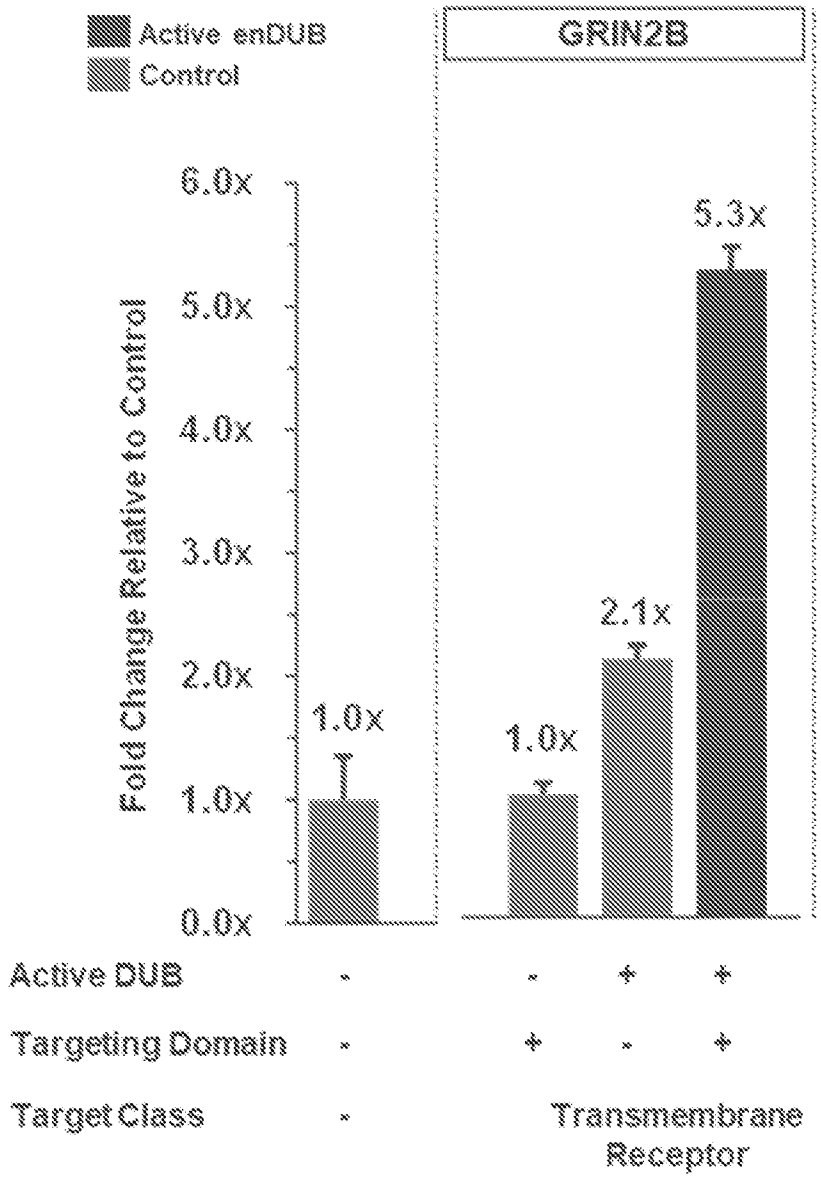

Active enDUB
Control
GRIN2B
Fold Change Relative to Control
6.0x
5.0x
4.0x
3.0x
2.0x
1.0x
0.0x
1.0x
1.0x
2.1x
5.3x
Active DUB
Targeting Domain
Target Class
Transmembrane Receptor

FIG. 5

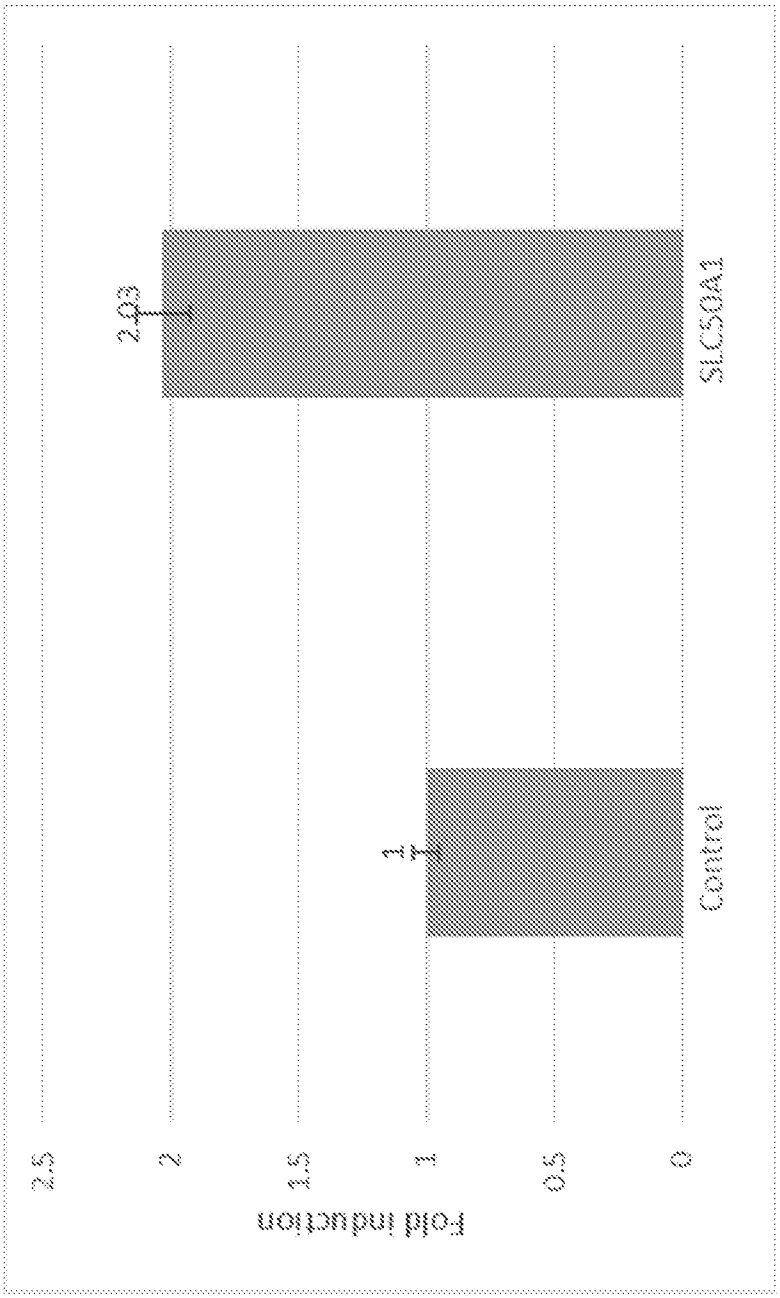


FIG. 6

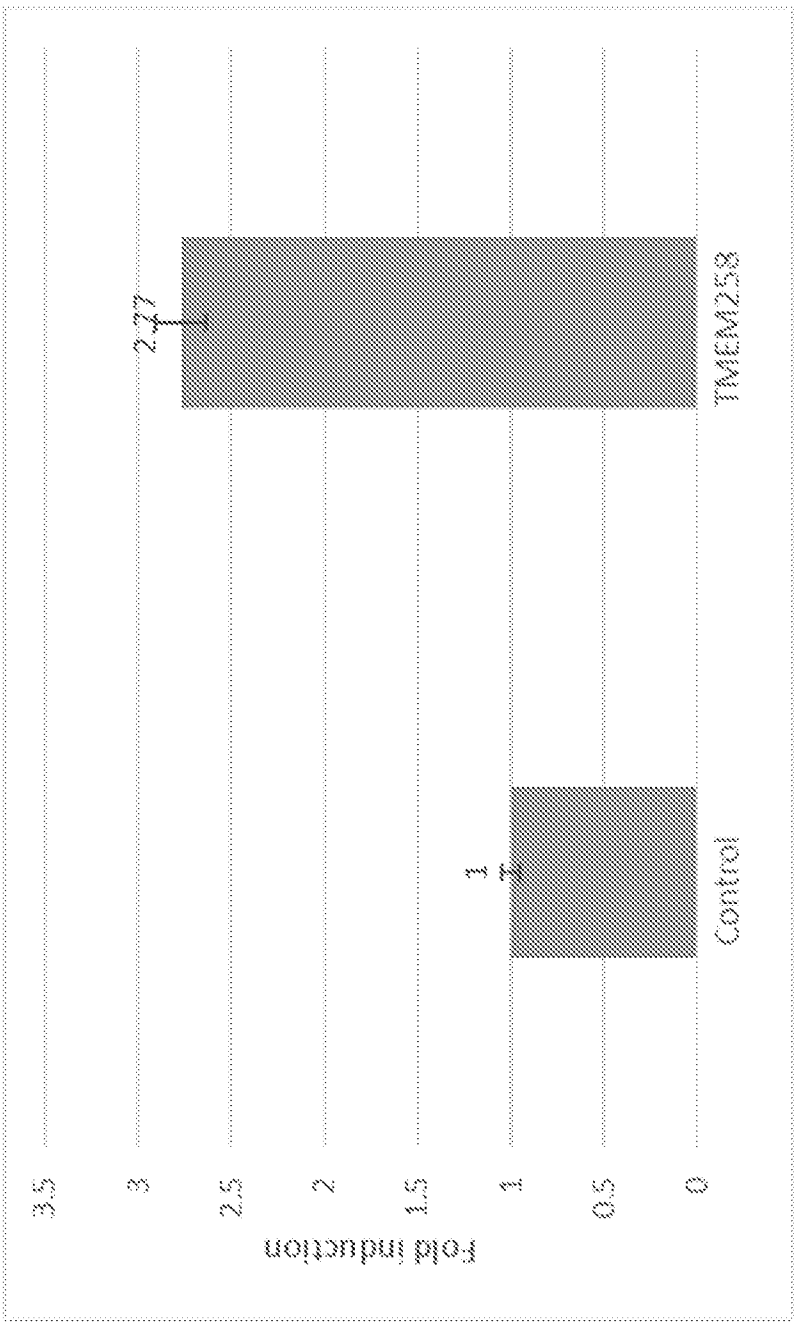


FIG. 7

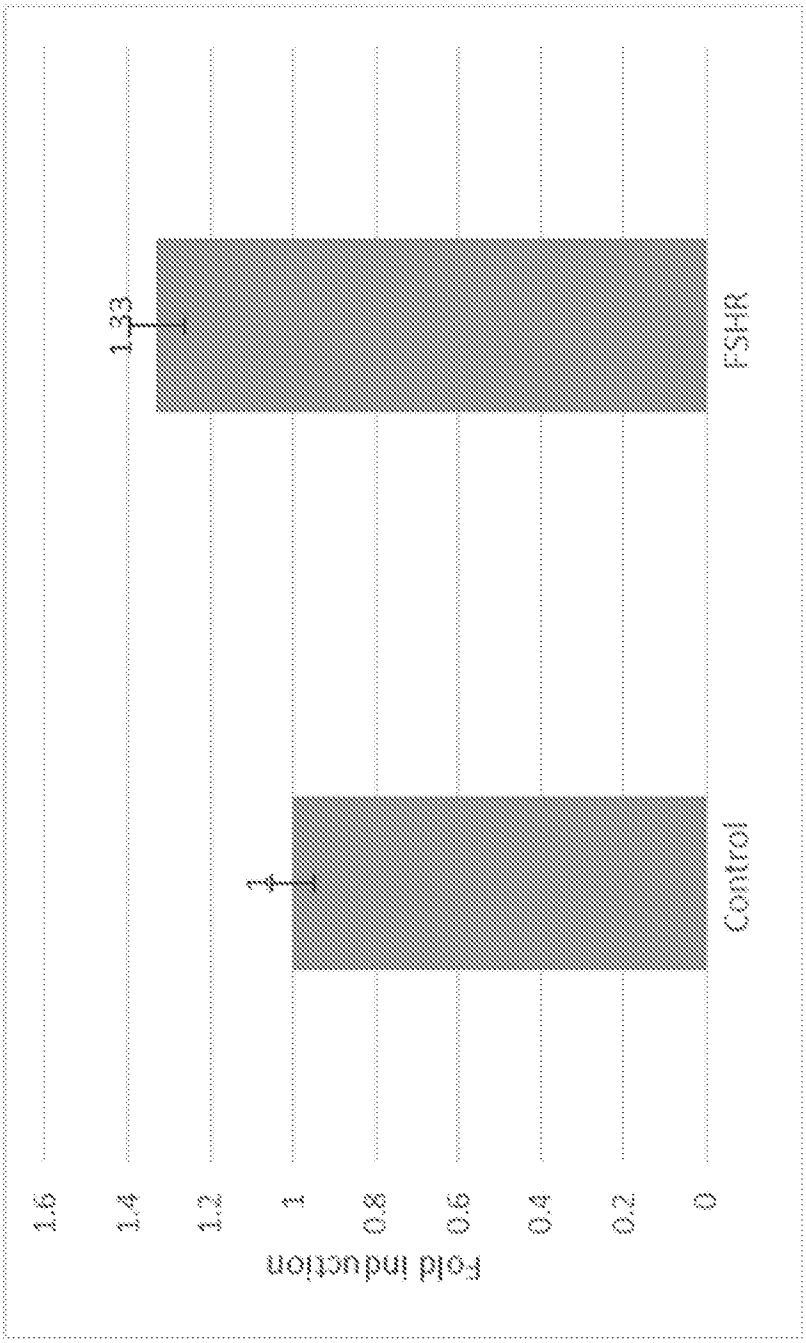


FIG. 8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2021/058291

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C07K 14/415; C12N 9/22; C12N 15/86 (2022.01)
CPC - C07K 14/415; C12N 9/22; C12N 15/86 (2022.02)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
see Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
see Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
see Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2019/126762 A2 (THE BROAD INSTITUTE INC. et al) 27 June 2019 (27.06.2019) entire document	1, 36
A	CN 101671688 A (SHANGHAI UNIVERSITY) 17 March 2010 (17.03.2010) machine translation	1, 36

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
05 April 2022	APR 18 2022
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Harry Kim. Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2021/058291

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☒ furnished subsequent to the international filing date for the purposes of international search only:

      ☒ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

SEQ ID NOs: 1, 228, and 265 were searched.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2021/058291

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 20-35, 41-94
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See extra sheet(s).

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1, 36

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2021/058291

Continued from Box No. III Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees need to be paid.

Group I+: claims 1-19 and 36-40 are drawn to fusion proteins.

The first invention of Group I+ is restricted to a fusion protein selected to be SEQ ID NO:265. It is believed that claims 1, and 36 read on this first named invention and thus these claims will be searched without fee to the extent that they read on SEQ ID NO:265.

Applicant is invited to elect additional fusion proteins, and their respective, corresponding, SEQ ID NOs to be searched in a specific combination by paying additional fee for each set of election. An exemplary election would be a fusion protein selected to be SEQ ID NO:266. Additional fusion proteins, and their respective, corresponding, SEQ ID NOs will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined.

The inventions listed in Groups I+ do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The Groups I+ formulas do not share a significant structural element responsible for treating genetic diseases requiring the selection of alternative fusion proteins where "The fusion protein of any one of the preceding claims, wherein said deubiquitinase comprises an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOS:1-11."

Additionally, even if Groups I+ were considered to share the technical features of a fusion protein comprising: a. an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof, and b. a targeting domain comprising a targeting moiety that specifically binds a membrane protein that is not an ion channel. However, these shared technical features do not represent a contribution over the prior art.

Specifically, WO 2019/126762 A2 to The Broad Institute Inc. et al. discloses a fusion protein (a fusion protein, Para. [0123]) comprising: a. an effector domain comprising a catalytic domain of a deubiquitinase, or a functional fragment or functional variant thereof, and b. a targeting domain comprising a targeting moiety that specifically binds a membrane protein that is not an ion channel (wherein the RNA targeting domain comprises a catalytically inactive Cpfl or Cpfl nickase protein, Para. [0036]; at least one or more half-monomers specifically ordered to target the genomic locus of interest linked to at least one or more effector domains are further linker to a chemical or energy sensitive protein, Para. [0553]; the functional domain may be selected from ...deubiquitinase, Para. [0174]; he domain may be derived from any membrane bound or transmembrane protein. Transmembrane regions of particular use in this disclosure may be derived from CD8, Para. [1663]).

The inventions listed in Groups I+ therefore lack unity under Rule 13 because they do not share a same or corresponding special technical features.