

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Supplementary information

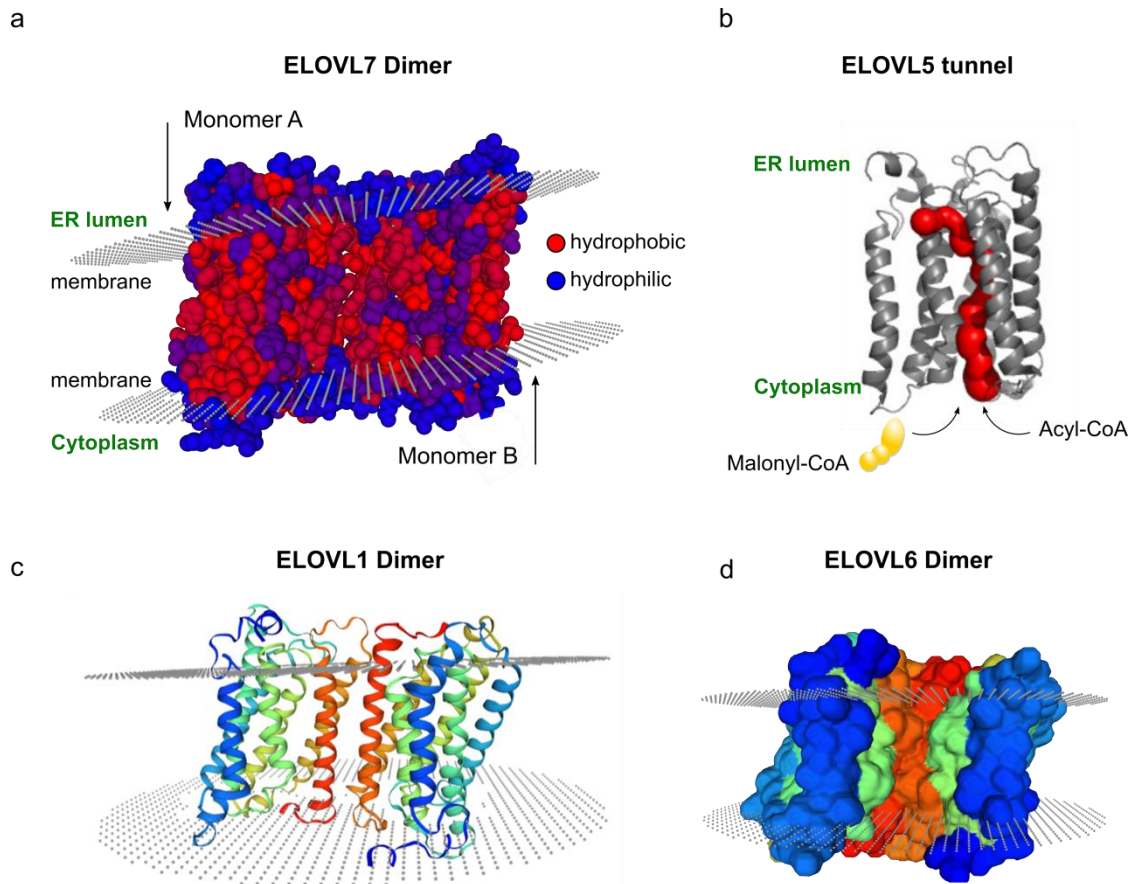
Enza Ferrero¹, Eleonora Di Gregorio², Marta Ferrero³, Erika Ortolan¹, Young-Ah Moon⁴, Antonella Di Campli^{5,6}, Lisa Pavinato¹, Cecilia Mancini^{1,7}, Debasmitha Tripathy⁸, Marta Manes⁹, Eriola Hoxha¹⁰, Chiara Costanzi¹¹, Elisa Pozzi¹, Matteo Rossi Sebastiano¹², Nico Mitro¹³, Filippo Tempia¹⁰, Donatella Caruso¹³, Barbara Borroni⁸, Manuela Basso⁹, Michele Salles¹⁴, Alfredo Brusco^{1,2}

1. Department of Medical Sciences, University of Torino, Torino, Italy
2. Unit of Medical Genetics, Città della Salute e della Scienza Hospital, Torino, Italy
3. Experimental Zooprophyllactic Institute of Piedmont, Liguria & Aosta Valley, Torino, Italy
4. Department of Molecular Medicine, Inha University College of Medicine, Incheon, South Korea
5. Institute of Protein Biochemistry, Italian National Research Council, Napoli, Italy
6. Department of Innovative Technologies in Medicine and Dentistry, G. d'Annunzio University of Chieti-Pescara, Chieti, Italy
7. Genetics and Rare Diseases Research Division, Bambino Gesù Children's Hospital, Rome, Italy
8. Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
9. Department of Cellular, Computational and Integrative Biology, University of Trento, Trento, Italy Neuroscience Institute Cavalieri Ottolenghi, Orbassano and Department of Neuroscience, University of Torino, Torino, Italy
10. Department of Neurology, Cremona Hospital, Cremona, Italy
11. Department of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Italy.
12. Department of Pharmacological and Biomolecular Sciences, University of Milan, Milan, Italy
13. Centre for Advanced Studies and Technology, G. d'Annunzio University of Chieti-Pescara, Chieti, Italy

The corresponding author is: Professor Alfredo Brusco, University of Torino, Department of Medical Sciences, Via Santena 19, 10126, Torino, Italy. Fax: +39 011 236 5926. Email: alfredo.brusco@unito.it

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

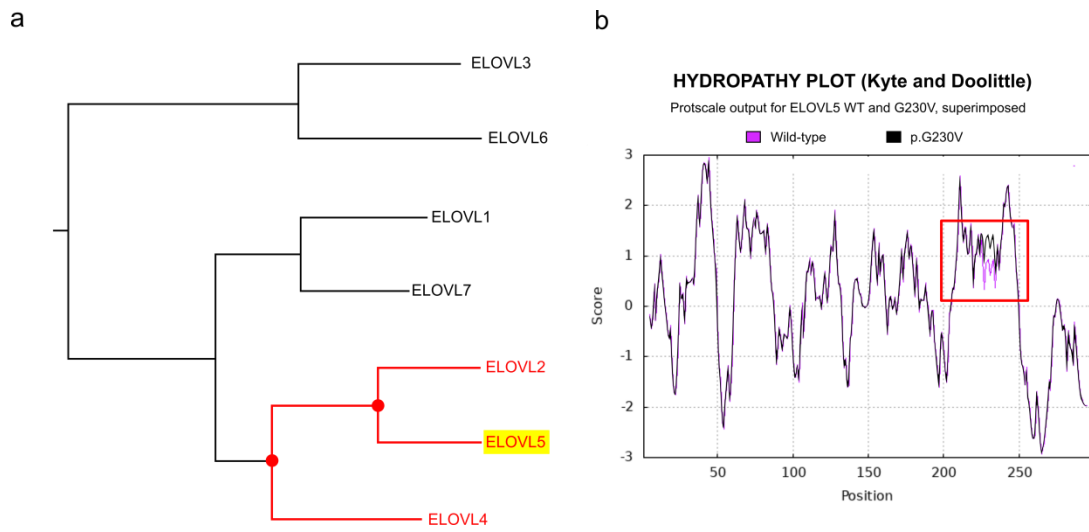


Supplementary Figure 1

Suppl. Fig. 1. Dimeric structure of human elongases. To date, three of the human elongases (ELOVL7, ELOVL1 and ELOVL6) are represented as homodimers in the Swiss-Model website (<https://swissmodel.expasy.org/>). (a) ELOVL7 homodimer (UniProtKB accession no. A1L3X0) is shown. Monomer A and B are represented in antiparallel array; hydrophobic or hydrophilic nature of the residues are indicated in this space-filling model. (b) Pore analysis of human ELOVL5 3D protein in PDBsum showing substrate-binding tunnel. The catalytic mechanism is a ping-pong type, two-step mechanism as described by Nie et al. (c) Cartoon model of ELOVL1 dimer (Q9BW60) with rainbow color scheme. (d) Surface model of ELOVL6 dimer (Q9H5J4) with rainbow color scheme.

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Ferrero et al.



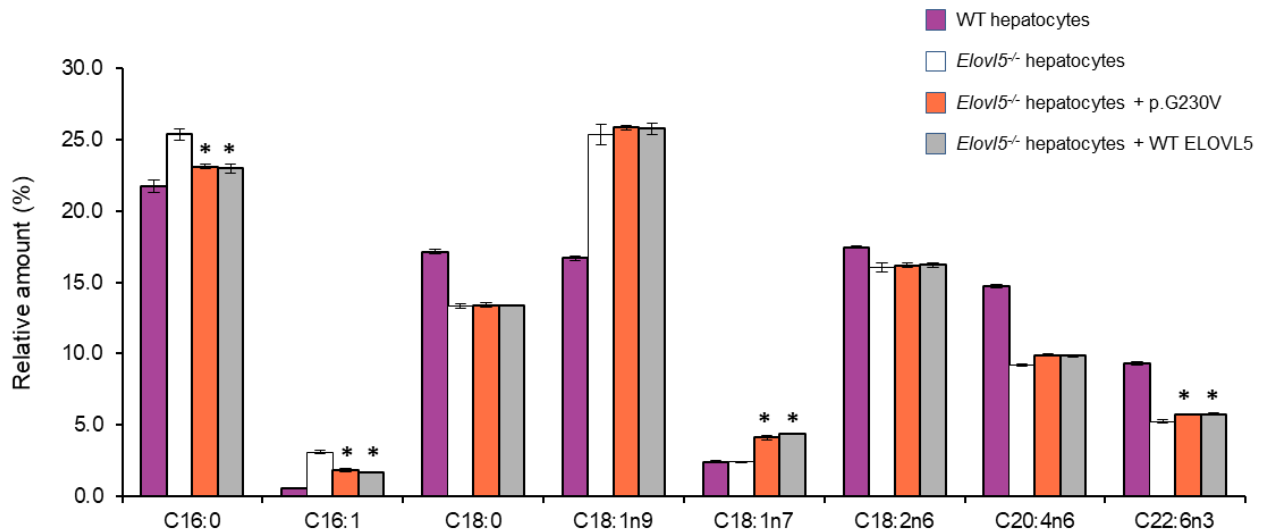
Supplementary Figure 2

Suppl. Fig. 2. (a) Neighbour-joining tree illustrating the phylogenetic relationship between the seven human ELOVL proteins. ELOVL2 and ELOVL4 proteins are the most closely related to ELOVL5, as highlighted by the red lines of the cladogram. The duplication nodes are indicated (●). Tree construction is detailed in the Materials and Methods. (b) Kyte-Doolittle hydropathy plot of wild-type (mauve line) and p.G230V (black line) ELOVL5 proteins showing increased hydrophobicity due to the G230V substitution.

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Supplementary Figure 3



Suppl. Fig. 3. Similar lipid profiles in hepatocytes from *Elov15*^{-/-} mice transfected with wild-type or variant ELOVL5. On day 0, primary hepatocytes were isolated from wild-type and *Elov15*^{-/-} mice. Cells were attached for 4 h and then infected with adenovirus to express either wild-type ELOVL5 or ELOVL5 p.G230V. ELOVL5 substrate fatty acids were not added to the medium. On day 2, lipids were extracted from the cells and whole cell lysates were prepared for protein expression and lipid composition as described in Moon et al., 2009. * indicates p<0.05 by Student t-test when comparing *Elov15*^{-/-} hepatocytes and *Elov15*^{-/-} hepatocytes + p.G230V or *Elov15*^{-/-} hep+WT ELOVL5. No difference was detected when comparing *Elov15*^{-/-} hepatocytes + p.G230V and *Elov15*^{-/-} hepatocytes + WT ELOVL5.

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Supplementary Table 1 Multiple sequence alignment of human ELOVL proteins

ELOVL1	----MEA-----VVNLYQEVMKHADPRIQGYPLMGSPLLMTSILLTY
ELOVL7	----MAF-----SDLTSRTVHLYDNWIKDADPRVEDWLLMSSPLPQTILLGFY
ELOVL2	----MEHL-----KAFDDEINAFLDNMFGPRDSRVRGWFMLDSYLPFTFFLTVMY
ELOVL5	----MEH-----FDASLSTYFKALLGPRDTRVKGWFLLDNYIPTFICSVIY
ELOVL4	----MGLLDSEPGSVLNVVSTALNDTVEFYRWTWSIADKRVENWPLMQSPWPTLSISTLY
ELOVL3	MVTAMNV-----SHEVNQLFQPYNFELS---KDMRPF-FEYEWATSFPIALIY
ELOVL6	----MM-----SVLT---LQEYEFQKFNENEAIQW-MQENWKKSFLFSALY
	* : :
ELOVL1	VYFVLSLGPRIANRKPQRLRGFMIVYNFSLVALSLY-----IVYEFLMSGWLSTYT
ELOVL7	VYFVTSLGPKLMENRKPFFELKKAMITYNFFIVLFSVY-----MCYEFVMSGWGIGYS
ELOVL2	LLSIW-LGNKYMKNRPAISLRGILTLYNLGITLLSAY-----MLAELILSTWEGGYN
ELOVL5	LLIIVW-LGPKYMRNKQPFSCRGILVVYNLGLTLLSLY-----MFCELVTVGWEGKYN
ELOVL4	LLFVW-LGPKWMDREPFQMRVLVLIYNFQGMVLLNLF-----IFRELFMGSYNAGYS
ELOVL3	LVLIA-VGQNYMKERKGFNLQGPLIILWSFCLAIFSIILGAVRMWIMGTVLLTGGLKQTV-
ELOVL6	AAFIF-GGRHLMNKRAKFEELRKLPLVLSLTLAVFSIFGALRTGAYMVYILMTKGLKQSV-
	: * . * . : : : : : : : : : : : :
ELOVL1	WRCDPVDYSNSPEALRMVRVAWLFLFSKFIELMDTVIFILRKKDGQVTFLHVVFHHSVLPW
ELOVL7	FRCDIVDYSRSPTALRMARTCWLYYFSKFIELLDTIFFVLRKKNSQVTFLHVVFHHTIMPW
ELOVL2	LQCQDLTTSAGEA-DIRVAKVLWVWYFYSKSVFELDTIFFVLRKKTSQITFLHVYHHASMFN
ELOVL5	FFCQGTRTAGES-DMKIRVWLWVWYFYSKLIIEFMDTFFFILRKNNHQITVFLHVYHHASMLN
ELOVL4	YICQSVSDYSNNVHEVRIAAALWVWYFVSKGVEYLDTVFFILRKKNNQVSVFLHVYHHCTMFT
ELOVL3	--CFINFDNST---VKFWSWVFLSKVIELGDTAFIILRKR--PLIFLHWYHHSTVLV
ELOVL6	--CDQGFYNGPV---SKFWAYAFVLSKAPELGDTIFILRQ--KLIFLHWYHHITVLL
	* : : . ** * ** : : : ** . : . : * : ** :
ELOVL1	SWWWGVKIAPGGMGSFHAMINSSVHVIMYLYYGLSAFGPVAQPYLWKKHMTAIQLIQFV
ELOVL7	TWWFVGVKFAAGGLGTFHALLNTAVHVMYSYYGLSALGPAYQKYLWKKYLTSLQLVQFV
ELOVL2	IWWCVLNIWPCGQSFPGPTLNSFIHILMYSYYGLSVF-PSMHKYLWKKYLTQAQLVQFV
ELOVL5	IWWFVMNVVPCGHSYFGATLNSFIHVLIMYSYYGLSSV-PSMRPYLWKKYITQGGQLLQFV
ELOVL4	LWWIGIKWVAGGQAFGAQLNSFIHVIMYSYYGLTAFGPWIQKYLWKKRYLTMLQLIQFH
ELOVL3	YTSFGYKKNKVPAGGWF-VTMNFGVHAIMYTYTLKAANVKPKML--PMLITSLQILQMF
ELOVL6	YSWYSYKDMVAGGWF-MTMNYGVHAVMYSYALRAAGFRVSRKF--AMFITLSQITQML
	: . . * : * : * : ** * * : : : * * : * :
ELOVL1	LVSLHISQYYFM---SSCNYQYFVIVHILWIMYGTIFFMFLFSNFWYHSYTK---GKRLP--
ELOVL7	IVAIHISQFFFFM---EDCKYQFPVFACIIMSYSFMFLLLFLHFWYRAYTK---GQRLP--
ELOVL2	LTITHTMSAVVK---PCGFPGCLI-FQSSYMLTLVILFLNFIYVQTY-----RKKPMK
ELOVL5	LTIIQTSQCGVIW---PCTFPLGWLY-FQIGYMISLIALFTNFYIQTYNKKGASRRKDHL
ELOVL4	VTIGHTALSLEYT---DCFPFKWMHW-ALIAAISFIPLFLNFIYIRTYKE---PKKPKAG
ELOVL3	VGAIVSILTYIWRQDQCCHTMEHLFWSFILY-MTYFILFAHFFCQTYIR---PKVKA--
ELOVL6	MGCVVNYLVFCWMQHDCCHSHFQNIWFSSLMY-LSYLVLFCHFFFEAYI---GKMRK--
	: * * . ** : : : . : * :
ELOVL1	RALQONGAPGIA-----KVKAN
ELOVL7	KTVKN-----GTC-----KNKDN
ELOVL2	KDMQE--PPAGKEVKNKGFSAKAYFTAANGVMNK--KAQ--
ELOVL5	KDHQN---GSMAAVNGHTNSFSPLENNVKPR--KLRKD
ELOVL4	KTAMN----GISANGVSKSEKQLMIENGGKQKNGKAKGD
ELOVL3	-----KTKSQ
ELOVL6	-----TTKAE
	. :

Multiple sequence alignment of human ELOVL1-7 aligned by MAFFT online program. Cysteine residues that form the conserved intramolecular disulfide bond connecting Loop 2 and Loop 6 are colored in cyan. The catalytic histidine-rich active site is showed in yellow. The green column contains the ELOVL5 G230 residue that is substituted to V230 in SCA38. The output order reflects the results of the alignment. Sequence accession numbers are: ELOVL1 (Q9BW60.1)

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

279aa; ELOVL2 (Q9NXB9.2) 296aa; ELOVL3 (Q9HB03.2) 270aa; ELOVL4 (Q9GZR5.1) 314aa; ELOVL5 (Q9NYP7.1) 299aa; ELOVL6 (Q9H5J4.1) 265aa; ELOVL7 (A1L3X0.1) 281aa.

Supplementary Table 2 Percent of amino acid sequence identity and similarity between the human ELOVL proteins

Amino Acid Identity (%)

ELOVL1	100						
ELOVL2	32.61	100					
ELOVL3	25.55	22.59	100				
ELOVL4	41.21	41.21	25.18	100			
ELOVL5	35.12	57.09	24.44	41.13	100		
ELOVL6	23.77	21.88	45.66	23.77	22.26	100	
ELOVL7	57.34	38.07	24.44	44.48	36.29	26.79	100
	ELOVL1	ELOVL2	ELOVL3	ELOVL4	ELOVL5	ELOVL6	ELOVL7

Amino Acid Similarity (%)

ELOVL1	100						
ELOVL2	45.16	100					
ELOVL3	36.29	35.18	100				
ELOVL4	51.61	54.05	38.14	100			
ELOVL5	47.31	68.24	39.25	53.84	100		
ELOVL6	35.09	34.71	56.22	35.84	36.98	100	
ELOVL7	69.53	45.55	36.29	54.44	45.19	38.49	100
	ELOVL1	ELOVL2	ELOVL3	ELOVL4	ELOVL5	ELOVL6	ELOVL7

The percent amino acid identity and similarity were calculated using the SIAS programme as detailed in the methods.

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Supplementary Table 3 Links or addresses of webservers/databases used in this study

Ataxia website:	https://neuromuscular.wustl.edu/ataxia/domatax.html
NCBI PDB structure database:	https://www.ncbi.nlm.nih.gov/structure/
NCBI Protein sequence database	https://www.ncbi.nlm.nih.gov/protein/
Mafft protein sequence alignment and tree	https://mafft.cbrc.jp/alignment/server/
SIAS percent aa sequence identity & similarity	http://imed.med.ucm.es/Tools/sias.html
Pfam protein family database	https://www.ebi.ac.uk/interpro/
Protter proteoform visualization	https://wlab.ethz.ch/protter/start/
Phyre2 protein modelling	http://www.sbg.bio.ic.ac.uk/~phyre2/html/page.cgi?id=index
UCSF Chimera protein modelling	https://www.cgl.ucsf.edu/chimera/
I-Mutant protein stability predictor	https://folding.biofold.org/i-mutant/i-mutant2.0.html
MAESTRO protein stability predictor	https://biwww.che.sbg.ac.at/
INPS-MD prediction server	https://inpsmd.biocomp.unibo.it/welcome/default/index
SAAFEC-SEQ stability predictor	http://compbio.clemson.edu/SAAFEC-SEQ/
I-Tasser protein modelling	https://zhanggroup.org/I-TASSER/
Swiss Model protein modelling	https://swissmodel.expasy.org/
AlphaFold Protein Structure Database	https://alphafold.ebi.ac.uk/
Kyte & Doolittle Hydropathy plot	https://web.expasy.org/protscale/
Human genomic variant search engine	https://varsome.com
PDBsum protein structure database	http://www.ebi.ac.uk/thornton-srv/databases/pdbsum/

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Supplementary Table 4 ELOVL5 Protein sequences used to generate the MSA

	Accession no.	Species	Length (Amino acids)
1	Q9NYP7.1	<i>Homo sapiens</i> (Human)	299
2	NP_599016.2	<i>Mus musculus</i> (Mouse)	299
3	NP_599209.1	<i>Rattus norvegicus</i> (Rat)	299
4	NP_001040062.1	<i>Bos taurus</i> (Bovine)	299
5	NP_001186126.1	<i>Gallus gallus</i> (Chicken)	295
6	NP_001011248.1	<i>Xenopus tropicalis</i> (Frog)	295
7	NP_001306343.1	<i>Macaca fascicularis</i> (Macaque)	299
8	NP_001130024.1	<i>Salmo salar</i> (Salmon)	294
9	NP_001290303.1	<i>Larimichthys crocea</i> (Croaker)	294
10	NP_001297348.1	<i>Anas platyrhynchos</i> (Duck)	295
11	XP_036724720.1	<i>Balaenoptera musculus</i> (Blue whale)	299
12	XP_036269542.1	<i>Pipistrellus kuhlii</i> (Bat)	299
13	XP_007892243.1	<i>Callorhynchus milii</i> (Elephant shark)	290
14	XP_020389096.1	<i>Rhincodon typus</i> (Whale shark)	293
15	AFR36912.1	<i>Esox lucius</i> (Pike)	295
16	NP_956747.1	<i>Danio rerio</i> (Zebrafish)	291
17	JAV42152.1	<i>Castor canadensis</i> (Beaver)	299
18	BBL33563.1	<i>Hypoclinemus mentalis</i> (Sole)	294
19	XP_037750142.1	<i>Chelonia mydas</i> (Turtle)	295
20	XP_037638316.1	<i>Sebastes umbrosus</i> (Rockfish)	294
21	XP_037375770.1	<i>Talpa occidentalis</i> (Mole)	299
22	XP_037248229.1	<i>Falco rusticolus</i> (Falcon)	295
23	XP_037015462.1	<i>Artibeus jamaicensis</i> (Fruit bat)	299
24	XP_017512380.2	<i>Manis javanica</i> (Pangolin)	299
25	XP_036772263.1	<i>Manis pentadactyla</i> (Chinese pangolin)	299
26	KAF7246807.1	<i>Varanus komodoensis</i> (Komodo dragon)	295
27	XP_027457290.1	<i>Zalophus californianus</i> (Sea lion)	298
28	XP_035256991.1	<i>Anguilla anguilla</i> (Eel)	296
29	XP_033874880.1	<i>Acipenser ruthenus</i> (Sturgeon)	294
30	XP_019805339.1	<i>Tursiops truncatus</i> (dolphin)	295

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Supplementary Table 5 CLUSTAL format alignment by MAFFT (v7.490) of **ELOVL5** proteins

```
HumanElov15      --MEHFDASLSTYFKALLGPRDTRVKGWFLLDNYIPTFICSVIYLLIVVLGPKYMRNKQP
Macaca.NP_00130 --MEHFDASLSTYFKALLGPRDTRVKGWFLLDNYIPTFICSVIYLLIVVLGPKYMRNKQP
SeaLion.XP_0274  --MENFDASLSTYFKALLGPRDTRVKGWFLLDNYIPTFICSVIYLLIVVLGPKYMRNKQP
Bat.XP_03626954 --MEHFDASLSTYFKALLGPRDTRVKGWFLLDNYIPTFICSTIYLLIVVLGPKYMRNKQP
FruitBat.XP_037  --MENFDASLSTYFKAWLGPDRTRVKGWFLLDNYIPTFICSVIYLLIVVLGPKYMRNKQP
Mouse.NP_599016 --MEHFDASLSTYFKAFGLGPRDTRVKGWFLLDNYIPTFVCSVIYLLIVVLGPKYMRNKQP
Rat.NP_599209.1 --MEHFDASLSTYFRALLGPRDTRVKGWFLLDNYIPTFVCSAIYLLIVVLGPKYMRNKQP
Beaver.JAV42152 --MENFDASLSTYFRAWLGPDRTRVKGWFLLDNYIPTFVCSVIYLLIVVLGPKYMRNKQP
Pangolin.XP_017  --MENFDASLSTYFKALLGPRDTRVKGWFLLDNYIPTFICSVIYLLIVVLGPKYMRNKQP
ChPangolin.XP_0  --MENFDASLSTYFKALLGPRDTRVKGWFLMDNYIPTFICSVIYLLIVVLGPKYMRNKQP
Mole.XP_0373757  --MENFDASLSTYFKALLGPRDTRVKGWFLLDNYIPTFICSVIYLLIVVLGPKYMRNKQA
Bos.NP_00104006 --MEHFDASLSTYFRAWLGPDRTRVEGWFLLDNYVPTLVCSILYLLIVVLGPKYMRNKQP
BlueWhale.XP_03  --MEHFDASLSTYFQALLGPRDLRVKGWFLLDNYIPTLLCSILYLLIVVLGPKYMRNKRP
Dolphin.XP_0198  --MEHFDASLSTYFQALLGPRDPRVKGWFLLDNYIPTLLCSILYLLIVVLGPKYMRNKRP
Gallus.NP_00118  --MERLDKTIINSYLDVWLGPRDPRVKGWLLLDNYPTTFIFSVLYLLIVVLGPKYMRNKQP
Duck.NP_0012973  --MERLDKTIINSYLDVWLGPRDPRVKGWLLLDNYPTTFIFSVLYLLIVVLGPKYMRNKQP
Falcon.XP_03724  --MEFLDKTIINSYLDVWLGPRDPRVKGWLLLDNYPTTFIFSVLYLLIVVLGPKYMRNKQP
Turtle.XP_03775  --MESLDQTIINSYLDVWFGPRDPRVKGWLLLDNYIPTTFIFSVLYLLIVVLGPKYMRNKQP
Komodo.KAF72468  --MESLDKTIINSYLDVWLGPRDPRVKGWLLLDNYPTTFIFSVLYLLIVVLGPKYMRNKQP
Xenopus.NP_0010  --MEVLDKAVNGYIDHLLGPKDPRVRGWLLLDNYVPTILFTALYLFIVWRGPKYMRNKRP
Salmo.NP_001130  --MEAFNHKLNTYIDSWMGPRDERVQGWLLLDNYPTTFALTMVYLLIVVLGPKYMRNRQP
Pike.AFR36912.1  --METFNQRLNTYIDSWMGPRDPRVKGWLLLDNYPTTFALTVIYLLIVVWAGPKYMRNRQP
Croaker.NP_0012  --METFNHKLNTYIDSWMGPRDQVRGWLLLDNYPTTFALTMVYLLIVVWAGPKYMRNRQP
Rockfish.XP_037  --METFNHKLNTYIDSWMGPRDQVRGWLLLDNYPTTFALTMVYLLIVVWAGPKYMRNRQP
AmSole.BBL33563  --METFNHKLNTYIDSWMGPRDQVRGWLLLDNYPTTFALTMVYLLIVVWAGPKYMRNRQP
Eel.XP_03525699  MDMEMFNHKLNTYIDSWMGPRDQVRGWLLLDNYPTTFALTMVYLLIVVWAGPKYMRNRQP
Sturgeon.XP_033  --MEALNQATNAYIDSWMGPRDTRVRGWFLLDNYPTTFVTVVLLYLFVWVWAGPKYMRNKQP
Zebrafish.NP_95  --METFSHRVNSYIDSWMGPRDLRVGTGWFLLDNYIPTTFIFVTVVYLLIVVWAGPKYMRNRQA
Eshark.XP_00789  --MGFADQTLNSYFDSWFGPRDPRVEGFLLLDNYPTTFLLTLIYLFVWVWAGPKYMRNKAP
WhaleShark.XP_0  --MEAVDRTLNYFVSWFGPRDSRVEGFLLDKYPTTFILSLLYLFVWVWAGPKYMRNKAP
      * . . . : : ** : * * * : * : . : * : * : * * : * : .

HumanElov15      FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGKYNFFCQGTRTAGESDMKIIRVLWVWYF
Macaca.NP_00130  FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGKYNFFCQGTRTAGESDMKIIRVLRWVYF
SeaLion.XP_0274  FSCRGILVLYNLGLTLLSLYMFCELVTVGWEGRYNFFCQGTRTAGESDMKIIRVLWVWYF
Bat.XP_03626954 LACRKILVVYNLGLTLLSLYMFCELVTVGWEGQYNFFCQGTRTAGESDMKIIRVLWVWYF
FruitBat.XP_037  FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGKYNFFCQGTRTAGESDMKIIRVLWVWYF
Mouse.NP_599016 FSCRGILQLYNLGLTLLSLYMFCELVTVGWEGKYNFFCQGTRTAGESDMKIIRVLWVWYF
Rat.NP_599209.1 FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGKYNFFCQGTRTAGESDMKIIRVLWVWYF
Beaver.JAV42152 FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGKYNFFCQGTRTAGESDMKIIRVLRWVYF
Pangolin.XP_017  FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGRYNFFCQGTRSSGEADVIVVLWVWYF
ChPangolin.XP_0  FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGRYNFFCQGTRSSGEADVIVVLWVWYF
Mole.XP_0373757  FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGKYNFFCQDTRTAGESDMKIIRVLRWVYF
Bos.NP_00104006 FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGQYNFFCQGTRSSGEADMKIIRVLRWVYF
BlueWhale.XP_03  FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGQYNFFCQGTRSSGEADMKIIRVLRWVYF
Dolphin.XP_0198 FSCRGILVLYNLGLTLLSLYMFCELVTVGWEGQYNFFCQGTRSSGEADMKIIRVLRWVYF
Gallus.NP_00118 FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGGYNFYFCQDTHSGGEADMKIIRVLRWVYF
Duck.NP_0012973 FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGGYNFYFCQDTHSGGEADMKIIRVLRWVYF
Falcon.XP_03724 FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGGYNFYFCQDTHSGGEADMKIIRVLRWVYF
Turtle.XP_03775 FSCRGILVVYNVGLTLLSLYMFCELVTVGWEGGYNFYFCQDTHSGGEADMKIIRVLRWVYF
Komodo.KAF72468 FSCRGILVVYNLGLTLLSLYMFCELVTVGWEGGYNFYFCQDTHSGGEADMKIIRVLRWVYF
Xenopus.NP_0010 VSCRGILVVYNLGLTLLSLYMFCELVTVGWEGGYNFYFCQDTHSGGEADMKIIRVLRWVYF
Salmo.NP_001130 VSCQGLLVLYNLALTLTLLSFMFYEMVSAVWQGGYNFYFCQDTHSAGETDTKIINVLWVWYF
Pike.AFR36912.1 LSCRGFLVVYNLGLTLLSLYMFCELVTVGWEGGYNFYFCQDTHSAGETDTKIINVLWVWYF
Croaker.NP_0012 YSCRGLLVLYNLGLTLLSFMFYELVTVAVWHGGYNFYFCQDTHSAGETDTKIINVLWVWYF
Rockfish.XP_037 YSCRGLLVLYNLGLTLLSFMFYELVTVAVRHGGYNFYFCQDTHSAGETDTKIINVLWVWYF
AmSole.BBL33563 YSCRGLLVVYNLGLTLLSFMFYELVTVAVWHGGYNFYFCQDTHSAGETDTKIINVLWVWYF
Eel.XP_03525699 FSCRGLLVVYNLGLTLLSLYMFCELVNGMWQGGYNFYFCQDTHSAGETDTKIINVLWVWYF
Sturgeon.XP_033 FSCRGVLLVVYNLGLTLLSFMFYELVTVGAWQGGYNFYFCQDTHSGGEADMKIIRVLRWVYF
Zebrafish.NP_95 YSCRALLVLYNLGLTLLSFMFYELVTVGAWQGGYNFYFCQDTHSGGEADMKIIRVLRWVYF
Eshark.XP_00789 VSCRGTLVVYNLGLTLLSLYMFCELVTVGWEGGYNFYFCQDTHSAGKADLKIIRVLRWVYF
WhaleShark.XP_0 LSSRGILVVYNLGLTLLSLYMFCELVTVGWVWGGYNFYFCQDTHSAGKADLKIIRVLRWVYF
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Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

::: * **: *:***:*** *: : . * * :*: . . . * :*:** ****

HumanElov15 SKLIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Macaca.NP_00130 SKLIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
SeaLion.XP_0274 SKLIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Bat.XP_03626954 SKLIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
FruitBat.XP_037 SKLIEFMDTFFFILRKNNHQVTVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Mouse.NP_599016 SKLIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Rat.NP_599209.1 SKLIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Beaver.JAV42152 SKLIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Pangolin.XP_017 SKLIEFMDTFFFILRKNNHQITVLHVYHHVSMMLNIWWFVMNWVPCGHSYFGATLNSFIHV
ChPangolin.XP_0 SKLIEFMDTFFFILRKNNHQITVLHVYHHVSMMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Mole.XP_0373757 SKLIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Bos.NP_00104006 SKLIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
BlueWhale.XP_03 SKLIEFMDTFFFILRKNNHQVTVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Dolphin.XP_0198 SKLIEFMDTFFFILRKNYHQVTVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Gallus.NP_00118 SKLIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Duck.NP_0012973 SKLIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Falcon.XP_03724 SKLIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Turtle.XP_03775 SKLIEFMDTFFFILRKNYHQITVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Komodo.KAF72468 SKLIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Xenopus.NP_0010 SKLIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Salmo.NP_001130 SKVIEFMDTFFFILRKNNHQITFLHYHHASMLNIWWFVMNWVPCGHSYFGASLNSFVHV
Pike.AFR36912.1 SKLIEFMDTFFFILRKNNHQITFLHYHHASMLNIWWFVMNWVPCGHCYFGACLNSFIHV
Croaker.NP_0012 SKLIEFMDTFFFILRKNNHQITFLHYHHASMLNIWWFVMNWVPCGHSYFGASLNSFVHV
Rockfish.XP_037 SKLIEFMDTFFFIVRKNNHQITFLHYHHASMLNIWWFVMNWVPCGHSYFGASLNSFVHV
AmSole.BBL33563 SKLIEFMDTFFFILRKNNHQITFLHYHHASMLNIWWFVMNWVPCGHSYFGASLNSFVHV
Eel.XP_03525699 SKLIEFMDTFFFILRKNNHQITFLHVYHHASMPSIWWFVMNWVPCGHSYFGASLNSFIHV
Sturgeon.XP_033 SKLIEFMDTFFFILRKNNHQITFLHVYHHATMPNIWWFVMNWVPCGHSYFGASFNFSFIHV
Zebrafish.NP_95 SKLIEFMDTFFFILRKNNHQITFLHVYHHATMLNIWWFVMNWVPCGHSYFGATLNSFIHV
Eshark.XP_00789 SKVIEFMDTFFFILRKNYHQITILHVYHHATMFNIWWFVMNWVPCGHSYFGATLNSFIHV
WhaleShark.XP_0 SKVIEFMDTFFFILRKNYHQITVLHVYHHATMFNIWWFVMNWVPCGHSYFGATLNSFIHV
:*:***:*** :*:**:*:*** :* .*****:**** :*** :***:***

HumanElov15 LMYSYGLSSVPSMRPYLWKKYITQGQLLQFVLTIIQTS CGVIWPCFPLGWLYFQIGY
Macaca.NP_00130 LMYSYGLSSVPSMRPYLWKKYITQGQLLQFVLTIIQTS CGVIWPCFPLGWLYFQIGY
SeaLion.XP_0274 LMYSYGLSSVPSVRPYLWKKYITQGQLLQFVLTIIQTS CGVLWPCFPLGWLYFQIGY
Bat.XP_03626954 LMYSYGLSSVPSMRPYLWKKYITQGQLI QFVLTIIQTT CGVIWPCSFPLGWLYFQIGY
FruitBat.XP_037 LMYSYGLSSVPSMRPYLWKKYITQGQLLQFVLTIVQTS CGVWPCSFPLGWLYFQIGY
Mouse.NP_599016 LMYSYGLSSI PSMRPYLWKKYITQGQLVQFVLTIIQTT CGVFWPCSFPLGWLFQIGY
Rat.NP_599209.1 LMYSYGLSSVPSMRPYLWKKYITQGQLVQFVLTIIQTS CGVIWPCSFPLGWLYFQIGY
Beaver.JAV42152 LMYSYGLSSVPSMRPYLWKKYITQGQLI QFVLTIIQTS CGVLWPCSFPLGWLYFQIGY
Pangolin.XP_017 LMYSYGLSSVPSMRPYLWKKYITQGQLLQFVLTIIQTS CGVWVPCFPLGWLYFQIGY
ChPangolin.XP_0 LMYSYGLSSVPSMRPYLWKKYITQGQLLQFVLTIIQTS CGVWPCAFPLGWLYFQIGY
Mole.XP_0373757 LMYSYALSSVPSMRPYLWKKYITQGQLLQFVLTIIQTT CGVIWRCFPLGWLYFQIGY
Bos.NP_00104006 LMYSYGLSSI PSMRPYLWKKYITQGQLLQFVLTIIQTS CGVIWPCFPLGWLYFQIGY
BlueWhale.XP_03 LMYSYGLSSVPSMRPYLWKKYITQGQLLQFVLTIIQTS CGVIWPCAFPLGWLYFQIGY
Dolphin.XP_0198 LMYSYGLSSVPSMRPYLWKKYITQGQLVQFVLTIIQTS CGVIWPCAFPLGWLYFQIGY
Gallus.NP_00118 LMYSYGLSAVPAMRPYLWKKYITQGQLI QFVLTIFQTS CGVWPCAFPLGWLYFQIFY
Duck.NP_0012973 LMYSYGLSAVPAMRPYLWKKYITQGQLTQFVLTIFQTS CGVWPCAFPLGWLYFQISY
Falcon.XP_03724 LMYSYGLSAVPAMRPYLWKKYITQGQLI QFVLTIFQTS CGVWPCAFPLGWLYFQISY
Turtle.XP_03775 LMYSYGLSAIPAMRPYLWKKYITQGQLI QFVLTIFQTS CGVWPCAFPLGWLYFQIFY
Komodo.KAF72468 LMYSYGLSAIPSMRPYLWKKYITQGQLI QFVLTIFQTS CGVWPCFPLGWLYFQIGY
Xenopus.NP_0010 LMYSYGLSAIPAMRPYLWKKYITQ CQLTQFVLTMTQTTCAMIWPCFPMGWLYFQNCY
Salmo.NP_001130 LMYSYGLSAVPAIRPYLWKKYITQGQLI QFFLTMSQTI CAVIWPCGFPFGWLFQIFY
Pike.AFR36912.1 LMYSYGLSAIPTMRPYLWKKYITQGQLI QFFLTMTQTI CAVIWPCGFPFGWLYFQISY
Croaker.NP_0012 VMYSYGLSAIPAMRPYLWKKYITQ LQLTQFFLTMSQTLCAVWPCGFPFGWLYFQISY
Rockfish.XP_037 VMYSYGLSAIPAIRPYLWKKYITQ FQLI QFFLTMTQTMCAVWPCGFPFGWLSFQISY
AmSole.BBL33563 VMYSYGLSAIPAMRPYLWKKYITQ LQLI QFFLTVSHTMCAVIWPCGFPFGWLFQISY
Eel.XP_03525699 LMYSYGLSAVPALRPYLWKKYITQ GQLI QFVMTMTQTS CAVWPCGFPFGWLYFQISY
Sturgeon.XP_033 LMYSYGLSAIPAVRPYLWKKYITQ GQLI QFVLTMTQTTCAVFRPCGFPFGWLYFQICY
Zebrafish.NP_95 LMYSYGLSAVPALRPYLWKKYITQ GQLVQFVLTMTQTS CAVWPCGFPFGWLYFQISY
Eshark.XP_00789 LMYSYGLSAIPAMRPYLWKKYITQ GQLLQFVMTIIQTS FGVWPCGFPFGWLYFQIGY

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

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WhaleShark.XP_0 LMYSYYGLSAIPAMRPLYLWKKYITQGGQLLQFVLTIIQTSFGVIWPCGFPSGWL YFQIGY
:*****.**:::*****:**** * * *.:* : * .:. * * * * * * * *
HumanElov15 MISLIALFTNFYIQTYNKKGASRRKDHLKDHQNGSMAAVNGHTNSFSPLENNVKPRKLRK
Macaca.NP_00130 MISLIALFTNFYIQTYNKKGASRRKDHLKDHQNGSVAAVNGHTNSFSPLENNVKPRKLRK
SeaLion.XP_0274 MISLITLFTNFYVQTYNKKGASRRKEHLKDHQNGSVAAVNGHTNSF-SLENNVKPRKQQRK
Bat.XP_03626954 MISLITLFTNFYIQTYNKKGASRRKEHLKDHQNGSLTAANGHTNSFSLENNVKLRKQQRK
FruitBat.XP_037 MISLILFTNFYIQTYNKKGASRRKERLRDHQNGSVTAANGHTNSFSLSLGNSTKPRKQQRK
Mouse.NP_599016 MISLIALFTNFYIQTYNKKGASRRKDHLKGHQNGSVAAVNGHTNSFPSENVKPRKQQRK
Rat.NP_599209.1 MISLIALFTNFYIQTYNKKGASRRKEHLKGHQNGSMTAVNGHTNNFASLENSVTSRKQQRK
Beaver.JAV42152 MISLIALFTNFYIQTYNKKGASRRDHLKDHQNGSATVNGHTNTFSSLENNVKPRKQQRK
Pangolin.XP_017 MISLIVLFTNFYVQTYNKKGASRRREYLKDHQNGSMAAMNGHAGSFSSLSGSAKPRKLRK
ChPangolin.XP_0 MISLIVLFTNFYVQTYNKKGASRRREYLKDHQNGSMAAVNGHAGSFSSLSGNSVKPRKLRK
Mole.XP_0373757 MISLITLFTNFYIQTYNKKGASRRKEHLKEHQNGSVAAVNGHTNSFSTLENNVKLRKQQRK
Bos.NP_00104006 MISLITLFTNFYIQTYNKKGVSRREHQKDHQNGSVAAVNGHISSFSLENNVKPRKQQRK
BlueWhale.XP_03 MISLIALFTNFYIQTYNKKGASRRREHQKDHQNGSVTAVNGHTSSFSLENNVKPRKQQRK
Dolphin.XP_0198 MISLIALFTNFYIQTYNKKGASRRRE----HQNGSVTAVNGHTSSFSLEHNSVKPRKQQRK
Gallus.NP_00118 MISLILFTNFYIQTYNKKASRRKE----YQNGSTATVNGYTNSFSLENNVKQQRKQQRK
Duck.NP_0012973 MISLILFTNFYIQTYNKKASRRKE----YQNGSAATVNGYTNSFSLENNVKQQRKQQRK
Falcon.XP_03724 MISLILFTNFYIQTYNKKASRRKE----YQNGSTATVNGYTNSSSSLENNVKQQRKQQRK
Turtle.XP_03775 MISLILFTNFYIQTYKKKASRRKE----YQNGSTAANGYTNSFSLENNVKQQRKQQRK
Komodo.KAF72468 MITLILFTNFYIQTYNKKAAACRRKE----YQNGSTAANGYTNSFSLENNVKQQRKQQRK
Xenopus.NP_0010 MISLILFGNFYIKTYNKKTSRRKE----YQNGSASAVNGHTNSFSLEDNVVKQQRKQQRK
Salmo.NP_001130 MASLIAFFSNFYIQTYKKHRVSQKEY----HQNGSVDSLNGHANGVTPTE-TITHRKVRV
Pike.AFR36912.1 MVTLIALFSNFYIQTYKKRSVSQKKEC----HRNGSASPLNGHVSGVTPTE-TITHRKVRA
Croaker.NP_0012 MVTLIFLFSNFYVQTYKKHSVSLKKE----HQNGSPVSTNGHANGTPSLE-HAAHKKLRV
Rockfish.XP_037 MVTLIFLFSNFYIQAYKKHSGSLKKE----HQNGSPISTNGHANGTPSME-RTAYQKLRM
AmSole.BBL33563 MVTLILFSNFYIQTYQKHSRSLQKD----HRNGSPASRNHANGKPSAE-QPAHKKLRV
Eel.XP_03525699 MVTLIALFSNFYIQTYQKQGAFFRRKE----HQNGSAAAMNGHNSNGVSPAELDLTRKLRV
Sturgeon.XP_033 LIVLIVLFSNFYIQTYKKRGSRRKE----CQNGSAAASLNGHANGVSSVD-NVTQRKLRK
Zebrafish.NP_95 MVTLILFSNFYIQTYKKRSGRKSD----YPNGS---VNGHTNGVMSSE-KIKHRKARA
Eshark.XP_00789 MISLIVLFTNFYIQTYQKKSASRTKD----CLNGS---ANGHTNGFSAQTDHYSAKKTH-
WhaleShark.XP_0 MISLILFTNFYIQTYKKKSAFKSKD----CLNGSTIAANGHTNGLSTQMDHYSEKKTTH-
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HumanElov15 D
Macaca.NP_00130 D
SeaLion.XP_0274 D
Bat.XP_03626954 D
FruitBat.XP_037 D
Mouse.NP_599016 D
Rat.NP_599209.1 D
Beaver.JAV42152 D
Pangolin.XP_017 D
ChPangolin.XP_0 D
Mole.XP_0373757 D
Bos.NP_00104006 D
BlueWhale.XP_03 D
Dolphin.XP_0198 D
Gallus.NP_00118 D
Duck.NP_0012973 D
Falcon.XP_03724 D
Turtle.XP_03775 D
Komodo.KAF72468 D
Xenopus.NP_0010 D
Salmo.NP_001130 D
Pike.AFR36912.1 D
Croaker.NP_0012 D
Rockfish.XP_037 D
AmSole.BBL33563 D
Eel.XP_03525699 D
Sturgeon.XP_033 D
Zebrafish.NP_95 D
Eshark.XP_00789 -
WhaleShark.XP_0 -
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Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Supplementary Table 6 ELOVL2 Protein sequences for Multiple Sequence Alignment

	Accession no.	Species	Length (AA)
1	Q9NXB9.2	<i>Homo sapiens</i> (Human)	296
2	XP_028703673.1	<i>Macaca mulatta</i> (Rhesus macaque)	296
3	NP_062296.1	<i>Mus musculus</i> (Mouse)	292
4	XP_032740498.1	<i>Rattus norvegicus</i> (Rat)	296
5	XP_027380089.1	<i>Bos indicus</i> x <i>Bos taurus</i> (Bovine)	294
6	NP_001184237.1	<i>Gallus gallus</i> (Chicken)	297
7	NP_001016159.1	<i>Xenopus tropicalis</i> (Frog)	296
8	NP_001130025.1	<i>Salmo salar</i> (Salmon)	287
9	XP_027307376.1	<i>Anas platyrhynchos</i> (Duck)	296
10	XP_007900820.1	<i>Callorhynchus milii</i> (Elephant shark)	300
11	XP_036725964.1	<i>Balaenoptera musculus</i> (Blue whale)	295
12	AGR34076.1	<i>Oncorhynchus masou</i> (Cherry salmon)	287
13	XP_005162628.1	<i>Danio rerio</i> (Zebrafish)	295
14	ETE65396.1	<i>Ophiophagus hannah</i> (King cobra)	301
15	XP_036301996.1	<i>Pipistrellus kuhlii</i> (Bat)	296

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Supplementary Table 7 MSA of ELOVL5 (30 sequences) and ELOVL2 (15 Sequences)

CLUSTAL format alignment by MAFFT (v7.505) Blosum 62/L-INS-i/Gap open penalty 1.53

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HumanElov15 -----MEHFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICSVIYLLIVWLGPKY
Macaca.NP_00130 -----MEHFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICSVIYLLIVWLGPKY
SeaLion.XP_0274 -----MENFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICSVIYLLIVWLGPKY
Bat.XP_03626954 -----MEHFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICSTIYLLIVWLGPKY
FruitBat.XP_037 -----MENFDASLSTYFKAWLGPDRVKGWFLLDNYIPTFICSVIYLLIVWLGPKY
Mouse.NP_599016 -----MEHFDASLSTYFKAFLLGPRDRVKGWFLLDNYIPTFVCSVIYLLIVWLGPKY
Rat.NP_599209.1 -----MEHFDASLSTYFRALLGPRDRVKGWFLLDNYIPTFVCSAIYLLIVWLGPKY
Beaver.JAV42152 -----MENFDASLSTYFRAWLGPDRVKGWFLLDNYIPTFVCSVIYLLIVWLGPKY
Pangolin.XP_017 -----MENFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICSVIYLLIVWLGPKY
ChPangolin.XP_0 -----MENFDASLSTYFKALLGPRDRVKGWFLMDNYIPTFICSVIYLLIVWLGPKY
Mole.XP_0373757 -----MENFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICSVIYLLIVWLGPKY
Bos.NP_00104006 -----MEHFDASLSTYFRAWLGPDRVEGWFLLDNYVPTLVCSILYLLIVWLGPKY
BlueWhale.XP_03 -----MEHFDASLSTYFQALLGPRDLRVKGWFLLDNYIPTLLCSILYLLIVWLGPKY
Dolphin.XP_0198 -----MEHFDASLSTYFQALLGPRDRVKGWFLLDNYIPTLLCSILYLLIVWLGPKY
Gallus.NP_00118 -----MERLDKTINSYLDVWLGPRDRVKGWLLLENYPTTFIFSVLYLLIVWLGPKY
Duck.NP_0012973 -----MERLDKTINSYLDVWLGPRDRVKGWLLLENYPTTFIFSVLYLLIVWLGPKY
Falcon.XP_03724 -----MEFLDKTINSYLDVWLGPRDRVKGWLLLENYPTTFIFSVLYLLIVWLGPKY
Turtle.XP_03775 -----MESLDQTINSYLDVWFGPRDRVKGWLLLDNYIPTFIFSVLYLLIVWLGPKY
Komodo.KAF72468 -----MESLDKTINSYLDVWLGPRDRVKGWLLLDNYPTTFIFSVLYLLIVWLGPKY
Xenopus.NP_0010 -----MEVLDKAVNGYIDHLLGPKDPRVRGWLLLDNYVPTILFTALYLFIVWRGPKY
Salmo.NP_001130 -----MEAFNHKLNTYIDSWMGPRDERVQGWLLLDNYPTTFALTMYLLIVWLGPKY
Pike.AFR36912.1 -----METFNQRNLNTYIDSWMGPRDERVRGWLLLDNYPTTFALTMYLLIVWAGPKF
Croaker.NP_0012 -----METFNHKLNTYLESWVGPRDQVRGWLLLDNYPTTFALTVMYLLIVWVGPKY
Rockfish.XP_037 -----METFNHRLNTYLESWVGPRDQVRGWLLLDNYPTTFALTMYLLIVWVGPKY
AmSole.BBL33563 -----METFNHKLNTYIDSWLGPDRQVRGWLLLDNYPTTFALTVMYLLIVWLGPKY
Eel.XP_03525699 -----MD-MEMFNHRLNTYIDSWMGPRDQVRGWLLLDNYPTTFALTVMYLLIVWVGPKY
Sturgeon.XP_033 -----MEALNQATNAYIDSWMGPRDRVRGWFLLDNFSPTVVLTLTYLFFVWVGPKY
Zebrafish.NP_95 -----METFSHRVNSYIDSWMGPRDLRVTGWFLLDNYIPTFIFTVMYLLIVWVGPKY
Eshark.XP_00789 -----MGFADQTLNSYFDNSWFGPRDRVEGFLLLDNYPTFLLTLTYLFFVWVGPKY
WhaleShark.XP_0 -----MEAVDRTLNYYFVSWFGPRDRSRVEGFLLDKYPTFILLSLTYLFFVWVGPKY
Macaca.XP_02870 -----MEHLKAFDDEINAFLDNMFGRDRSRVWGFMLDSYLPTFFLTVIYLLSIWLGPKY
Human.sp|Q9NXXB9 -----MEHLKAFDDEINAFLDNMFGRDRSRVWGFMLDSYLPTFFLTVMYLLSIWLGPKY
XP_036301996.1 -----MELLKAFDDKINAFLDNMFGRDRSRVWGFMLDSYLPTFFSLTVMYLLSIWLGPKY
Bos.XP_02738008 -----MEHLKAFDDEVNAFLDNMFGRDRSRVWGFMLDSYLPTFFSLTVLYLLSIWLGPKY
Bwhale.XP_03672 -----MEHLKAFDDEINAFLDNMFGRDRSRVWGFMLDSYLPTFFSLTVLYLLSIWLGPKY
Rat.XP_03274049 -----MEQLKAFDNEVNAFLDNMFGRDRSRVWGFLLDSYLPTFTLTITMYLLSIWLGPKY
Mouse.NP_062296 -----MEQLKAFDNEVNAFLDNMFGRDRSRVWGFLLDSYLPTFILTITTYLLSIWLGPKY
Gallus.NP_00118 -----MEHLKAFDQEVNAFVDYMFGRDARVRGWLLLDNYLPTFFLTVAYLLCIWLGPKY
Duck.XP_0273073 -----MEHLKAFDQEVNAFVDYMFGRDRSRVWGFLLDSYLPTFFLTCAYLLCIWLGPKY
Frog.NP_0010161 -----MEHIEKIDQEVNAFVDYLFGRDTRTRGWMLLDNYLPTFFLTLTYLFLSIWLGPKY
Shark.XP_007900 M MPTVANQIETLDRKRVNSFVDYMFGRDRSRVWGFMLDSYLPTFFLTLTYLFLSIWLGPKY
ETE65396.1 -----MEHIEKIDQEVNAFVDYLFGRDTRTRGWMLLDNYLPTFFLTLTYLFLSIWLGPKY
Salmo.NP_001130 -----MNHLQSLDERLNKLFYFLFEDRDRSRVWGFLLDSYLPTLSLTIYLLSVYLGSKY
Cherry -----MNHLQSLDERLNALFYFLFEDRDRSRVWGFLLDSYLPTLSLTIYLLSVYLGSKY
Zebrafish.XP_00 -----MESYEKIDKLLNSVVDLSLFGDRDRSRVWGFLLDSYPTFFLTIYLLSVYLGSKY
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HumanElov15 MRNKQPFSCRGILVVYNLGLTLLSLYMFCE-----LVTGVWEG
Macaca.NP_00130 MRNKQPFSCRGILVVYNLGLTLLSLYMFCE-----LVTGVWEG
SeaLion.XP_0274 MKNRQPFSCRGILVLYNLGLTLLSLYMFCE-----LVKGVWEG
Bat.XP_03626954 MKNRQPLACRKILVVYNLGLTLLSLYMFCE-----LVTGVWEG
FruitBat.XP_037 MKNRQPFSCRGILVVYNLGLTLLSLYMFCE-----LVTGVWEG
Mouse.NP_599016 MKNRQPFSCRGILQLYNLGLTLLSLYMFYE-----LVTGVWEG
Rat.NP_599209.1 MKNRQPFSCRGILVVYNLGLTLLSLYMFYE-----LVTGVWEG
Beaver.JAV42152 MKNRQPFSCRGILVVYNLGLTLLSLYMFYE-----LVTGVWEG
Pangolin.XP_017 MKNRQPFSCRGILVVYNLGLTLLSLYMFYE-----LVTGVWEG
ChPangolin.XP_0 MKNRQPFSCRGILVVYNLGLTLLSLYMFYE-----LVTGVWEG
Mole.XP_0373757 MKNRQAFSCRGILVVYNLGLTLLSLYMFCE-----LVTGVWEG
Bos.NP_00104006 MKTRQPFSCRGILVVYNLGLTLLSLYMFCE-----LVTGVWEG
BlueWhale.XP_03 MKNRPPFSCRGILVVYNLGLTLLSLYMFCE-----LVTGVWEG
Dolphin.XP_0198 MKNRPPFSCRGILVLYNLGLTLLSLYMFCE-----LVTGVWEG
Gallus.NP_00118 MRNKQPFSCRGILVVYNLGLTLLSLYMFYE-----LVTGVWEG

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Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

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Duck.NP_0012973 MRNKQPFSCRGILVVYNLGLTLLSLYMFYE-----LVTGVWEG
Falcon.XP_03724 MRNKQPFSCRGILVVYNLGLTLLSLYMFYE-----LVTGVWEG
Turtle.XP_03775 MQNKQPFSCRGILVVYNVGLTLLSLYMFYE-----LVTGVWEG
Komodo.KAF72468 MQKRPPFSCRGILVVYNLGLTLLSLYMFYE-----LVTGVWEG
Xenopus.NP_0010 MQNRPPVSCRGILVVYNLGLTLLSLYMFYE-----LVTGVWEG
Salmo.NP_001130 MRHRQPVSCQGLLVLYNLALTLLSFYMFYE-----MVASVWQG
Pike.AFR36912.1 MRHRQPLSCRGFLVVYNLGLALLSLYMFSE-----MVASVWVG
Croaker.NP_0012 MKHRQPYSCRGLLVLYNLGLTLLSFYMFYE-----LVTAVWHG
Rockfish.XP_037 MKHRQPYSCRGLLVLYNLGLTLLSFYMFYE-----LVS AVRHG
AmSole.BBL33563 MKHRQPYSCRGLLVVYNLGLTLLSFYMFYE-----LVGAVWHG
Eel.XP_03525699 MKNRQPFSCRGLLVVYNLGLTLLSMYFCE-----LVNGMWQG
Sturgeon.XP_033 MKNKEPFSCRGLVVVYNLGLTLLSFYMFYE-----LVNGAWQG
Zebrafish.NP_95 MKNRQAYSCRALLVPYNLCLTLLSLYMFYE-----LVMSVYQG
Eshark.XP_00789 MKNKAPVSCRGTLVVYNI GLTLLSLYMFYE-----LLTGVWEG
WhaleShark.XP_0 MQNKAPLSSRGILVVYNI GLTLLSLYMFCE-----LVRGVWDG
Macaca.XP_02870 MKNRPALSLRGILTLYNLGITLLSAYMLAE-----LILSTWEG
Human.sp|Q9NXB9 MKNRPALSLRGILTLYNLGITLLSAYMLAE-----LILSTWEG
XP_036301996.1 MKNRPALSLRSILTLYNLGITLLSMYMLAE-----LILSTWEG
Bos.XP_02738008 MRNRPALSLRGILTLYNLGITLLSAYMLAE-----LILSSWEG
Bwhale.XP_03672 MRSRAALSLRGILTLYNLGITLLSAYMLAE-----LILSSWEG
Rat.XP_03274049 MKNRPALSLRGILTLYNLGITLLSAYMLVE-----LVLSSWEG
Mouse.NP_062296 MKNRPALSLRGILTLYNLAITLLSAYMLVE-----LILSSWEG
Gallus.NP_00118 MKNRQPFSLKAHLIVYNLGITLLSLYMLIE-----LILATWEG
Duck.XP_0273073 MKNRPPFSLRAHLIVYNLGITLLSMYMLIE-----LILATWEG
Frog.NP_0010161 MQNRPAFSLRGHLIVYNLVVTLLSLYMLIE-----LILSTWEG
Shark.XP_007900 MKDRPAFFLRTHLIIYNLGVMLLSYMFIE-----LILSSWEG
ETE65396.1 MKNRPALSLRGLLIVYNFVTVLSFYMLIEVRLNRRILNFLFLAFYSADWDLILATWEG
Salmo.NP_001130 MRNRPAYSLKGVLVQVYNFVVTMLSLYMLVE-----LVSATLSA
Cherry MRNRPAYSLKGVLVQVYNFVVTMLSLYMLVE-----LVLATLSA
Zebrafish.XP_00 MRNRPAYSLKNVLLLYNFVTVLSFYMLVE-----LISAVWSA
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HumanElovl5 KYNFFCQGTRTAGESDMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHAS
Macaca.NP_00130 KYNFFCQGTRTAGESDMKI IRVLRWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHAS
SeaLion.XP_0274 RYNFFCQGTRSAGEADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHAS
Bat.XP_03626954 QYNFFCQGTRSAGEADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHAS
FruitBat.XP_037 KYNFFCQGTRSAGEADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHAS
Mouse.NP_599016 KYNFFCQGTRSAGESDMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHATM
Rat.NP_599209.1 KYNFFCQGTRSAGESDMKIVRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHATM
Beaver.JAV42152 KYNFFCQGTRSAGESDMKI IQVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHAS
Pangolin.XP_017 RYNFFCQGTRSSGADVIVRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHVSM
ChPangolin.XP_0 RYNFFCQGTRSSGADVIVRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHVSM
Mole.XP_0373757 KYNFFCQDTRSAGEADMKI IHVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHAS
Bos.NP_00104006 QYNFFCQGTRSGEADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHAS
BlueWhale.XP_03 QYNFFCQGTRSRGADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHAS
Dolphin.XP_0198 QYNFFCQGTRSGEADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNYHQITVLHVYHHAS
Gallus.NP_00118 GYNFYCQDTHSGEADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHATM
Duck.NP_0012973 GYNFFCQDTHSGEADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHATM
Falcon.XP_03724 GYNFFCQDTHSGEADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHATM
Turtle.XP_03775 GYNFFCQDTHSGEADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNHYQITVLHVYHHAS
Komodo.KAF72468 GYNFFCQDTHSGEADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHATM
Xenopus.NP_0010 GYNFFCQDTHSGGDADTKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITVLHVYHHAS
Salmo.NP_001130 GYNFYCQDTHSAGETDTKI INVLWVWYFYSKLVIEFMDTFFFILRKNNHQITFLHIYHHAS
Pike.AFR36912.1 GYHFYCQDTRSAGEADTRI IHVLWVWYFYSKLIIEFMDTFFFILRKNNHQITFLHIYHHAS
Croaker.NP_0012 GYNFYCQDIHSAQEVNDKI INVLWVWYFYSKLIIEFMDTFFFILRKNNHQITFLHIYHHAS
Rockfish.XP_037 GYNFYCQDTHSAQEVNDKIMNVLWVWYFYSKLIIEFMDTFFFIVRKNNHQITFLHIYHHAS
AmSole.BBL33563 DYNFYCQNTHSAPVDKVINVLWVWYFYSKLIIEFMDTFFFILRKNNHQITFLHIYHHAS
Eel.XP_03525699 NYNFFCQDTHSAGEADTKI INVLWVWYFYSKLIIEFMDTFFFILRKNNHQITFLHVYHHAS
Sturgeon.XP_033 GYNFFCQDTHSGEADMKI IRVLWVWYFYSKLIIEFMDTFFFILRKNNHQITFLHVYHHATM
Zebrafish.NP_95 GYNFFCQNTHSGGDADNRMMNVLWVWYFYSKLIIEFMDTFFFILRKNNHQITFLHVYHHATM
Eshark.XP_00789 GYSIFCQDTHSAGADLKI IRVLWVWYFYSKLVIEFMDTFFFILRKNYHQITILHVYHHATM
WhaleShark.XP_0 GYSIFCQNTHNAGEADLKI IRVLWVWYFYSKLVIEFMDTFFFILRKNYHQITVLHVYHHATM
Macaca.XP_02870 GYNLQCQDLTSAGEADIRVAKVLWVWYFYSKSVEFLDTIFFVLRKKTSSQITFLHVYHHAS
Human.sp|Q9NXB9 GYNLQCQDLTSAGEADIRVAKVLWVWYFYSKSVEFLDTIFFVLRKKTSSQITFLHVYHHAS
XP_036301996.1 GYNLQCQDLASAGEADVIRVAKVLWVWYFYSKLIIEFLDTIFFVLRKKTSSQITFLHVYHHAS
```

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

```
Bos.XP_02738008 GYNLQCQDLTSAGEADIRVARVLWVWYFYSKLIIEFLDTIFFVLRKKTSQVTFVLHVVYHHAS  
Bwhale.XP_03672 GYNLQCQDLTSAGEADIRVAGVLWVWYFYSKLIIEFLDTIFFVLRKKTSQITFLHVVYHHAS  
Rat.XP_03274049 GYNLQCQNLDSAGEGDIRVAKVLWVWYFYSKLVIEFLDTIFFVLRKKTSQITFLHVVYHHAS  
Mouse.NP_062296 GYNLQCQNLDSAGEGDIRVAKVLWVWYFYSKLVIEFLDTIFFVLRKKTNQITFLHVVYHHAS  
Gallus.NP_00118 GYNLQCQNLHSAAGEADIRVAKVLWVWYFYSKVIEFADTIFVLRKKSSQITFLHVVYHHATM  
Duck.XP_0273073 GYNLQCQNLHSAAGAADIRVAKVLWVWYFYSKVIEFMDTIFVLRKKSSQITFLHVVYHHATM  
Frog.NP_0010161 GYNLQCQNLDSAGKADVRVAKVLWVWYFYSKAEIEFMDTIFVLRKKNSQITFLHVVYHHAS  
Shark.XP_007900 AYYLQCQNLHSAAGEVDIRVAKVLWVWYFYSKAVEFMDTIFVLRKKNSQITFLHVVYHHATM  
ETE65396.1 NYNLQCQNLISAGETDIRVARVLWVWYFYSKVIEFADTVFVLRKKNSQITFLHVVYHHATM  
Salmo.NP_001130 GYRLQCQGLHEAGEADLRVAKVLWVWYFYSKVIEFLDTIFFVLRKKNSQITFLHVVYHHAS  
Cherry GYRLQCQGLHEAGEADLRVAKVLWVWYFYSKVIEFLDTIFFVLRKKNSQITFLHVVYHHAS  
Zebrafish.XP_00 GYRLQCQALDEVGEADIRVAKVLWVWYFYSKLIIEFLDTIFFVLRKKNSQITFLHVVYHHAS  
* : ** * :: ** ***** :** **.*::** : *::**.***.***.***
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HumanElovl5 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLLQF  
Macaca.NP_00130 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLLQF  
SeaLion.XP_0274 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSVRPYLWVWKKYITQGQLLQF  
Bat.XP_03626954 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLLQF  
FruitBat.XP_037 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLLQF  
Mouse.NP_599016 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLVQF  
Rat.NP_599209.1 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLVQF  
Beaver.JAV42152 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLLQF  
Pangolin.XP_017 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLLQF  
ChPangolin.XP_0 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLLQF  
Mole.XP_0373757 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYALSSVPSMRPYLWVWKKYITQGQLLQF  
Bos.NP_00104006 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLLQF  
BlueWhale.XP_03 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLLQF  
Dolphin.XP_0198 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSSVPSMRPYLWVWKKYITQGQLVQF  
Gallus.NP_00118 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSAVPAMRPYLWVWKKYITQGQLLQF  
Duck.NP_0012973 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSAVPAMRPYLWVWKKYITQGQLTQF  
Falcon.XP_03724 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSAVPAMRPYLWVWKKYITQGQLLQF  
Turtle.XP_03775 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSAIPAMRPYLWVWKKYITQGQLLQF  
Komodo.KAF72468 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSAIPAMRPYLWVWKKYITQGQLLQF  
Xenopus.NP_0010 LNIWWFVMNWVPCGHSYFGATLNSFIHVLMSYYGLSAIPAMRPYLWVWKKYITQCQLTQF  
Salmo.NP_001130 LNIWWFVMNWVPCGHSYFGASLNSFVHVLMSYYGLSAIPAIRPYLWVWKKYITQGQLLQF  
Pike.AFR36912.1 LNIWWFVMNWVPCGHCFYFACLNSFIHVLMSYYGLSAIPTMRPYLWVWKKYITQGQLLQF  
Croaker.NP_0012 LNIWWFVMNWVPCGHSYFGASLNSFVHVVMYSYYGLSAIPAMRPYLWVWKKYITQLQLTQF  
Rockfish.XP_037 LNIWWFVMNWVPCGHSYFGASLNSFVHVVMYSYYGLSAIPAIRPYLWVWKKYITQGQLLQF  
AmSole.BBL33563 LNIWWFVMNWI PCGHSFFGASLNSFVHVVMYSYYGLSAIPAMRPYLWVWKKYITQLQLLQF  
Eel.XP_03525699 PSIWWFVMNWVPCGHSYFGASLNSFIHVLMSYYGLSAVPALRPYLWVWKKYITQGQLLQF  
Sturgeon.XP_033 PNIWWFVMNWVPCGHSYFGASLNSFIHVLMSYYGLSAIPAVRPYLWVWKKYITQGQLLQF  
Zebrafish.NP_95 LNIWWFVMNWVPCGHSYFGATFNSFIHVLMSYYGLSAVPALRPYLWVWKKYITQGQLVQF  
Eshark.XP_00789 LNIWWFVMNWVPCGHSFFGATLNSFIHVLMSYYGLSAIPAMRPYLWVWKKYITQGQLLQF  
WhaleShark.XP_0 FNIWWFVMNWVPCGHSFFGATLNSFIHVLMSYYGLSAIPAMRPYLWVWKKYITQGQLLQF  
Macaca.XP_02870 FNIWWCVLNWI PCGQSFFGPTLNSFIHILMSYYGLSVFSPMHKYLWVWKKYLTQAQLVQF  
Human.sp|Q9NXB9 FNIWWCVLNWI PCGQSFFGPTLNSFIHILMSYYGLSVFSPMHKYLWVWKKYLTQAQLVQF  
XP_036301996.1 FNIWWCVLNWI PCGQSFFGPTLNSFIHILMSYYGLSVFSPMHKYLWVWKKYLTQAQLVQF  
Bos.XP_02738008 FNIWWCVLNWI PCGQSFFGPTLNSFIHILMSYYGLSVFSPMHKYLWVWKKYLTQAQLVQF  
Bwhale.XP_03672 FNIWWCVLNWI PCGQSFFGPTLNSFIHILMYTYGLSVFSPMHKYLWVWKKYLTQAQLVQF  
Rat.XP_03274049 FNIWWCVLNWI PCGQSFFGPTLNSFIHILMSYYGLSVFSPMHRYLWVWKKYLTQAQLVQF  
Mouse.NP_062296 FNIWWCVLNWI PCGQSFFGPTLNSFIHILMSYYGLSVFSPMHKYLWVWKKYLTQAQLVQF  
Gallus.NP_00118 FNIWWCVLNWI PCGQSFFGPTLNSFIHVLMSYYGLSVIPSMRKYLWVWKKYLTQAQLLQF  
Duck.XP_0273073 FNIWWCVLNWI PCGQSFFGPTLNSFIHVLMSYYGLSVIPSMRKYLWVWKKYLTQAQLLQF  
Frog.NP_0010161 FNIWWCVLNWI PCGQSFFGPTLNSFIHVLMSYYGLSVIPSMHKYLWVWKKYLTQAQLVQF  
Shark.XP_007900 FNIWWCVLNWI PCGQSFFGPTLNSFIHVLMSYYGLSTIPSMQPYLWVWKKYLTQAQLVQF  
ETE65396.1 FNIWWCVMNWI PCGQSFFGPTLNSFIHILMSYYGLSVIPSMRKYLWVWKKYLTQAQLLQF  
Salmo.NP_001130 FNIWWCVLNWI PCGQSFFGPTLNSFIHVCMSYYGLSTIPSMQKYLWVWKKYLTQAQLLQF  
Cherry FNIWWCVLNWI PCGQSFFGPTLNSFIHVCMSYYGLSTIPSMQKYLWVWKKYLTQAQLLQF  
Zebrafish.XP_00 FNIWWCVLNWI PCGQSFFGPTLNSFIHVLMSYYGLATIPSMHKYLWVWKKYLTQAQLVQF  
.*** *::**.***.***.*** *::**.***.***.*** *::**.***.***.*** *::**.***.***.***
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HumanElovl5 VLTIIQTSCGVIWPCFPLGWLIFYQIGYMISLIALFTNFYIQTYNKKGASRRKDKHLDHQ  
Macaca.NP_00130 VLTIIQTSCGVIWPCFPLGWLIFYQIGYMISLIALFTNFYIQTYNKKGASRRKDKHLDHQ  
SeaLion.XP_0274 VLTIIQTSCGVLWPCFPLGWLIFYQIGYMISLITLFTNFYVYQTYNKKGASRRKEHLKDHQ  
Bat.XP_03626954 VLTIIQTTCGVIWPCSFPLGWLIFYQIGYMISLITLFTNFYIQTYNKQASRRKEHLKDHQ
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Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

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FruitBat.XP_037 VLTIVQTSCGVVWPCSFPLGWLYLFQIGYMISLIIILFTNFYIQTYNKKGASRRKERLRDHQ
Mouse.NP_599016 VLTIIQTTCGVVWPCSFPLGWLYFFQIGYMISLIALFTNFYIQTYNKKGASRRKDHLKGHQ
Rat.NP_599209.1 VLTIIQTSCGVWPCSFPLGWLYLFQIGYMISLIALFTNFYIQTYNKKGASRRKEHLKGHQ
Beaver.JAV42152 VLTIIQTSCGVWPCSFPLGWLYLFQIGYMISLIALFTNFYIQTYNKKGASRRRDHLKDHQ
Pangolin.XP_017 VLTIIQTSCGVVWPCFPLGWLYLFQIGYMISLIVLFTNFYVQTYNKKGASRRREYLKDHQ
ChPangolin.XP_0 VLTIIQTSCGVVWPCAFPLGWLYLFQIGYMISLIVLFTNFYVQTYNKKGASRRREYLKDHQ
Mole.XP_0373757 VLTIIQTTCGVWPCFPLGWLYLFQIGYMISLITLFTNFYIQTYNKKGASRRKEHLKEHQ
Bos.NP_00104006 VLTIIQTSCGVWPCFPLGWLYLFQIGYMISLITLFTNFYIQTYNKKGVSRRREHQKDHQ
BlueWhale.XP_03 VLTIIQTSCGVWPCAFPLGWLYLFQIGYMISLIALFTNFYIQTYNKKGASRRREHQKDHQ
Dolphin.XP_0198 VLTIIQTSCGVWPCAFPLGWLYLFQIGYMISLIALFTNFYIQTYNKKGASRRRE----HQ
Gallus.NP_00118 VLTIFQTSCGVVWPCAFPLGWLYLFQIGYMISLIIILFTNFYIQTYNKKASRRKE----YQ
Duck.NP_0012973 VLTIFQTSCGVVWPCAFPLGWLYLFQIGYMISLIIILFTNFYIQTYNKKASRRKE----YQ
Falcon.XP_03724 VLTIFQTSCGVVWPCAFPLGWLYLFQIGYMISLIIILFTNFYIQTYNKKASRRKE----YQ
Turtle.XP_03775 VLTIFQTSCGVVWPCAFPLGWLYLFQIGYMISLIIILFTNFYIQTYNKKASRRKE----YQ
Komodo.KAF72468 VLTIFQTSCGVVWPCFPLGWLYLFQIGYMITLIIILFTNFYIQTYNKKACRRKE----YQ
Xenopus.NP_0010 VLTMTQTTCAMIWPCFPMGWLYLFQNCYMSLIIILFGNFYIKTYNKKTSRRKE----YQ
Salmo.NP_001130 FLTMSQTICAVIWPCGFPRGWLYFFQIFYMASLIAFFSNFYIQTYKKHRVSOKEY----HQ
Pike.AFR36912.1 FLTMTQTICAVIWPCGFPMGWLYLFQISYMTLIALFSNFYIQTYKKRSVSQKKEC----HR
Croaker.NP_0012 FLTMSQTLCAVVWPCGFPMGWLYLFQISYMTLIFLFSNFYVQTYKKHSVSLKKE----HQ
Rockfish.XP_037 FLTMTQTMCAVVWPCGFPMGWLYSFQISYMTLIFLFSNFYIQAYKKHSGSLKKE----HQ
AmSole.BBL33563 FLTVSHTMCAVIWPCGFPMGWLYFFQISYMTLIIILFSNFYIQTYQKHSRSLQKD----HR
Eel.XP_03525699 VMTMTQTSCAVVWPCGFPRGWLYLFQISYMTLIALFSNFYIQTYQKQGAFFRKE----HQ
Sturgeon.XP_033 VLTMTQTTCAVFRPCGFPMGWLYLFQICYLIVLIVLFSNFYIQTYKKRGSRRKE----CQ
Zebrafish.NP_95 VLTMTQTSCAVVWPCGFPMGWLYLFQISYMTLILLLFSNFYIQTYKKRSGSRKSD----YP
Eshark.XP_00789 VMTIIQTSGVVWPCGFPMGWLYLFQIGYMISLIVLFTNFYIQTYQKKSASRTKD----CL
WhaleShark.XP_0 VLTIIQTSGVIWPCGFPMGWLYLFQIGYMISLIIILFTNFYIQTYKKSAFKSKD----CL
Macaca.XP_02870 VLTIIHTMSAVVKPCGFPMGWLYLFQSSYMLTLVILFLNFYVQTYRKKPMKKDMQ----EP
Human.sp|Q9NXB9 VLTIIHTMSAVVKPCGFPMGWLYLFQSSYMLTLVILFLNFYVQTYRKKPMKKDMQ----EP
XP_036301996.1 VLTIIHTLSAVVKPCGFPMGWLYLFQSSYMLTLVILFLNFYVQTYRKKPMKKETE----EL
Bos.XP_02738008 LLTIIHTMSAVVRPCGFPMGWLYLFQSSYMLTLVILFLNFYVQTYRKKPMKKAME----E-
Bwhale.XP_03672 VLTIIHTMSAVVRPCGFPMGWLYLFQSSYMLTLVILFLNFYVQTYRKKPMKKDGE----EP
Rat.XP_03274049 VLTIIHTLSAVVKPCGFPMGWLYLFQSSYMLTLVILFLNFYVQTYRKKPKGKEMQ----EG
Mouse.NP_062296 VLTIIHTLSAVVKPCGFPMGWLYLFQSSYMLTLVILFLNFYVQTYRKKPVKKELO----E-
Gallus.NP_00118 LLTIVHTLSAAVKPCGFPMGWLYLFQSSYMATLVILFVNFYIKTYQKAPSRRTAAK----ET
Duck.XP_0273073 LLTIVHTLSAAVKPCGFPMGWLYLFQSSYMATLVILFVNFYIKTYRKAAPSRTAVK----ET
Frog.NP_0010161 LLTIIHTLSAAVKPCGFPMGWLYLFQSSYMATLVILFVNFYIKTYKRRPSKSDPN----GI
Shark.XP_007900 VLTIIHTVSAVVKPCGFPMGWLYLFQSSYMATLVILFVNFYVVKTYRKTVVQDNKT----N-
ETE65396.1 LLTIIHTLSAAVKPCGFPMGWLYLFQSSYMATLVVLFNFYVVKTYQKASAKANAK----EI
Salmo.NP_001130 ILTIIHTLSAIVVPCGFPMGWLYLFQSSYMATLVILFVNFYVQTYRKRPEES-----
Cherry ILTIIHTLSAIVVPCGFPMGWLYLFQSSYMATLVILFVNFYVQTYRKRPEES-----
Zebrafish.XP_00 VLTIIHTVSAVVVPCGFPLGWLYLFQTFYMCTLVVLFVNFYIQTYKRRKTEGGRM-----
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HumanElov15 NGSMAAVNGHTNSFSPLENNVK-PRKLRKD
Macaca.NP_00130 NGSVAAVNGHTNSFSPLENNVK-PRKLRKD
SeaLion.XP_0274 NGSVAAVNGHTNSF-SLENNVK-PRKQRKD
Bat.XP_03626954 NGSMTAANGHTNSFSLENNVK-LRKQRKD
FruitBat.XP_037 NGSVTAANGHTNSFSLGNSTK-PRKQRKD
Mouse.NP_599016 NGSVAAVNGHTNSFPLENSVK-PRKQRKD
Rat.NP_599209.1 NGSMTAVNGHTNNFASLENSVT-SRKQRKD
Beaver.JAV42152 NGSATVVNGHTNTFSSLENNVK-PRKQRKD
Pangolin.XP_017 NGSMAAMNGHAGSFSSLGSSAK-PRKLRKD
ChPangolin.XP_0 NGSMAAVNGHAGSFSSLGNSVK-PRKLRKD
Mole.XP_0373757 NGSVAAVNGHTNSFSTLENNVK-LRKQRKD
Bos.NP_00104006 NGSVAAVNGHISSFSSLENNVK-PRKQRKD
BlueWhale.XP_03 NGSVTAVNGHTSSFSSLENNVK-PRKQRKD
Dolphin.XP_0198 NGSVTAVNGHTSSFSSLEHSVK-PRKQRKD
Gallus.NP_00118 NGSTATVNGYTNSFSSLENNVK-QRKQRKD
Duck.NP_0012973 NGSAAVNGYTNSFSSLENNVK-QRKQRKD
Falcon.XP_03724 NGSTATVNGYTNSSSSLENNVK-QRKQRKD
Turtle.XP_03775 NGSTAAVNGYTNSFSSLENNVK-QRKQRKD
Komodo.KAF72468 NGSTAAVNGYTNSFSSLENNVK-QRKQRKD
Xenopus.NP_0010 NGSASAVNGHTNSFSSLEDNVK-QRKQRKD
Salmo.NP_001130 NGSVDSLNGHANGVTPTE-TIT-HRKVRVD
Pike.AFR36912.1 NGSASPLNGHVSGVTPTE-TIT-HRKVRAD
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Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Supplementary Table 8 ELOVL4 protein sequences for Multiple Sequence Alignment

	Accession no.	Species	Length (AA)
1	Q9GZR5.1	<i>Homo sapiens</i> (Human)	314
2	Q9EQC4.2	<i>Mus musculus</i> (Mouse)	312
3	XP_032765767.1	<i>Rattus norvegicus</i> (Rat)	314
4	AAI42460.1	<i>Bos taurus</i> (Bovine)	314
5	XP_046770079.1	<i>Gallus gallus</i> (Chicken)	314
6	XP_002936253.1	<i>Xenopus tropicalis</i> (Frog)	328
7	ADJ95235.1	<i>Salmo salar</i> (Salmon)	306
8	XP_001366145.1	<i>Monodelphis domestica</i> (Opossum)	314
9	XP_028902935.1	<i>Ornithorhynchus anatinus</i> (Platypus)	321
10	XP_007104948.1	<i>Physeter catodon</i> (Sperm whale)	314
11	XP_002714591.1	<i>Oryctolagus cuniculus</i> (Rabbit)	314
12	XP_008683076.1	<i>Ursus maritimus</i> (Polar bear)	314
13	XP_005299664.1	<i>Chrysemys picta bellii</i> (Painted turtle)	314
14	XP_011363206.1	<i>Pteropus vampyrus</i> (Large flying fox)	313
15	XP_026520959.1	<i>Notechis scutatus</i> (Tiger snake)	313

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Supplementary Table 9 MSA ELOVL5 (30 sequences) and ELOVL4 (15 Sequences)

CLUSTAL format alignment by MAFFT (v7.505) Method: L-INS-I, Blosom 62 matrix

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HumanElovl5 -----MEHFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICS
Macaca.NP_00130 -----MEHFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICS
SeaLion.XP_0274 -----MENFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICS
Bat.XP_03626954 -----MEHFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICS
FruitBat.XP_037 -----MENFDASLSTYFKAWLGPRDRVKGWFLLDNYIPTFICS
Mouse.NP_599016 -----MEHFDASLSTYFKAFLLGPRDRVKGWFLLDNYIPTFVCS
Rat.NP_599209.1 -----MEHFDASLSTYFRALLGPRDRVKGWFLLDNYIPTFVCS
Beaver.JAV42152 -----MENFDASLSTYFRALLGPRDRVKGWFLLDNYIPTFVCS
Pangolin.XP_017 -----MENFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICS
ChPangolin.XP_0 -----MENFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICS
Mole.XP_0373757 -----MENFDASLSTYFKALLGPRDRVKGWFLLDNYIPTFICS
Bos.NP_00104006 -----MEHFDASLSTYFRALLGPRDRVGEVWFLLDNYVPTLVCS
BlueWhale.XP_03 -----MEHFDASLSTYFQALLGPRDLRVKGWFLLDNYIPTLLCS
Dolphin.XP_0198 -----MEHFDASLSTYFQALLGPRDRVKGWFLLDNYIPTLLCS
Gallus.NP_00118 -----MERLDKTINSYLDVWLGPRDRVKGWLLLENYPTPTFIFS
Duck.NP_0012973 -----MERLDKTINSYLDVWLGPRDRVKGWLLLENYPTPTFIFS
Falcon.XP_03724 -----MEFLDKTINSYLDVWLGPRDRVKGWLLLENYPTPTFIFS
Turtle.XP_03775 -----MESLDQTINSYLDVWFGPRDRVKGWLLLDNYIPTFIFS
Komodo.KAF72468 -----MESLDKTINSYLDVWLGPRDRVKGWLLLTNYPTPTFIFS
Xenopus.NP_0010 -----MEVLDAVNGYIDHLLGPKDRVRGWLLLDNYVPTILFT
Salmo.NP_001130 -----MEAFNHKLNTYIDSWMGPRDERVQGWLLLDNYPPPTFALT
Pike.AFR36912.1 -----METFNQRLNTYIDSWMGPRDERVRGWLLLDNYPPPTFALT
Croaker.NP_0012 -----METFNHKLNTYLESWVGPRDQVRGWLLLDNYPPPTFALT
Rockfish.XP_037 -----METFNHRLNTYLESWVGPRDQVRGWLLLDNYPPPTFALT
AmSole.BBL33563 -----METFNHKLNTYIDSWLGPRDQVRGWLLLDNYPPPTFALT
Eel.XP_03525699 MD-----MEMFNHRLNTYIDSWMGPRDQVRGWLLLDNYPPPTFALT
Sturgeon.XP_033 -----MEALNQATNAYIDSWMGPRDRVRGWFLLDNFSPVTVLT
Zebrafish.NP_95 -----METFSHRVNSYIDSWMGPRDLRVTWGFLLDNYIPTFIFT
Eshark.XP_00789 -----MGFADQTLNSYFDSWFGPRDRVVEGFLLLDNYPPPTFLT
WhaleShark.XP_0 -----MEAVDRTLNSYFVSWFGPRDRSRVEGFLLLDNYPPPTFILS
sp|Q9GZR5.1|ELO -----
XP_008683076.1 MGL-----LDSEPGSVLNVVSTALNDTVEFYRWTW-SITDKRVENWPLMQSPWPTLCIS
XP_002714591.1 MGL-----LDSEPGSVLNVVSTALNDTVEFYRWTW-SIADKRVEDWPLMRSPWPTLSIS
sp|Q9EQC4.2|ELO -----
XP_032765767.1 MGL-----LDSEPGSVLNAVSTAFNDTVEFYRWTW-SIADKRVEDWPLMQSPWPTLSIS
XP_011363206.1 MGL-----LDSEPGSVLNVVSTALNDTVEFYRWTW-SITDKRVENWPLMQSPLPTLCIS
AAI42460.1 MGL-----LDSEPGSVLNAVSTALNDTVEFYRWTW-SITDKRVENWPLMQSPLPTLCIS
XP_007104948.1 MGL-----LDSEPGSVLNVVSTALNDTVEFYRWTW-SITDKRVENWPMMQSPLPTLCIS
XP_001366145.1 MGL-----LDAEPARMLDAVSTAVNDTIEFYRWTW-TIVDKRVENWPLMQSPLPTLCIS
XP_028902935.1 MEAPGAARPAALDALGALDAVSSALNGSLRFYRWTW-TIADKRVENWPLMQSPLPTLTIS
XP_046770079.1 MGA-----AAAEPRAAGLVSSVLDNTLEFYRWTW-SIRDKRVDDWPLMQSPFPPTLTIS
XP_005299664.1 MGS-----AAEQGRATGLVSSLLNDTLEFYRWSW-SIRDKRVDDWFLMQSPFPPTLTIS
XP_026520959.1 MGH-----SGEP-----GLIANVVNDTLEFYRWSW-TIRDKRVDDWPMMQSFPPTLIIS
XP_002936253.1 -----MLSPVSDVIQRTLQLYDWCF-SIADKRVEKWPLMQSPLPTLAIS
ADJ95235.1 -----MEAVTHFMNDTVEFYRWSL-TIADKRVEKWPMMSAPPTLAIS
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HumanElovl5 VIYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFCELVTVGWEGKYNFFCQGT
Macaca.NP_00130 VIYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFCELVTVGWEGKYNFFCQGT
SeaLion.XP_0274 VIYLLIVVWLGPKYMKNRQPFSCRGILVLYNLGLTLLSLYMFCELVKGVWEGRYNFFCQGT
Bat.XP_03626954 TIYLLIVVWLGPKYMKNRQPLACRKLIVVYINLGLTLLSLYMFCELVTVGWEGQYNFFCQGT
FruitBat.XP_037 VIYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFCELVTVGWEGKYNFFCQGT
Mouse.NP_599016 VIYLLIVVWLGPKYMKNRQPFSCRGILVLYNLGLTLLSLYMFYELVTVGWEGKYNFFCQGT
Rat.NP_599209.1 AIYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFYELVTVGWEGKYNFFCQGT
Beaver.JAV42152 VIYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFYELVTVGWEGKYNFFCQGT
Pangolin.XP_017 IYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFYELVTVGWEGRYNFFCQGT
ChPangolin.XP_0 IYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFYELVTVGWEGRYNFFCQGT
Mole.XP_0373757 VIYLLIVVWLGPKYMKNRQAFSCRGILVVYINLGLTLLSLYMFCELVTVGWEGKYNFFCQGT
Bos.NP_00104006 ILYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFCELVTVGWEGQYNFFCQGT
BlueWhale.XP_03 ILYLLIVVWLGPKYMKNRPPFSCRGILVVYINLGLTLLSLYMFCELVTVGWEGQYNFFCQGT
Dolphin.XP_0198 ILYLLIVVWLGPKYMKNRPPFSCRGILVLYNLGLTLLSLYMFCELVTVGWEGQYNFFCQGT
Gallus.NP_00118 VLYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFYELVTVGWEGGYNFFCQGT
Duck.NP_0012973 VLYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFYELVTVGWEGGYNFFCQGT
Falcon.XP_03724 VLYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFYELVTVGWEGGYNFFCQGT
Turtle.XP_03775 VLYLLIVVWLGPKYMKNRQPFSCRGILVVYINLGLTLLSLYMFYELVTVGWEGGYNFFCQGT
Komodo.KAF72468 VLYLLIVVWLGPKYMKNRPPFSCRGILVVYINLGLTLLSLYMFYELVTVGWEGGYNFFCQGT
Xenopus.NP_0010 ALYLLIVVWLGPKYMKNRPPVSCRGILVVYINLGLTLLSLYMFYELVTVGWEGGYNFFCQGT
Salmo.NP_001130 LMYLLIVVWLGPKYMRHRQPVSCQGLLVLYNLALTLTLLSYMFYEMVSAVWVGGYNYFCQGT
Pike.AFR36912.1 VIYLLIVVWAGPKFMRHRQPLSCRGFLVVYINLGLALLSLYMFSEMVAVWVGGYHFYFCQGT
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Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Croaker.NP_0012 VMYLVIVVMGPKYMKHRQPYSCRGLLVLYNLGLTLLSFYMFYELVTAVWHGGYNFYCQDI
Rockfish.XP_037 IMYLLIVVMGPKYMKHRQPYSCRGLLVLYNLGLTLLSFYMFYELVSAVRHGGYNFYCQDT
AmSole.BBL33563 VMYLLIVVWLGPKYMKHRQPYSCRGLLVVYNLGLTLLSFYMFYELVAVWHGDYNYFYCQNT
Eel.XP_03525699 VAYLLIVVMGPKYMKNRQPFSCRGLLVVYNLGLTLLSLYMFCELVNGMWQGNYNFFCQDT
Sturgeon.XP_033 LLYLFFVWVIGPKYMKNKEPFSCRGLLVVYNLGLTLLSFYMFYELVTGAWQGGYNFFCQDT
Zebrafish.NP_95 VMYLLIVVMGPKYMKNRQAYSCRALLVPYNLCLTLLSLYMFYELVMSVYQGGYNFFCQNT
Eshark.XP_00789 LIYLFFVWVAGPKYMKNKAPVSCRGLTVVYINIGLTLTLLSLYMFYELLTGVWEGGYSIFCQDT
WhaleShark.XP_0 LLYLFFVWVAGPKYMNKAPLSSRGILVVYINIGLTLTLLSLYMFCELVRVGVDGGYSIFCQNT
sp|Q9GZR5.1|ELO -----EPFQMLVLI IYNFGMVLLNLFIFRELFMGSYNAGYSYICQSV
XP_008683076.1 TLYLLFVWLGPKWMDREPFQMLVLI IYNFGMVLLNLFIFRELFMGSYNAGYSYICQSV
XP_002714591.1 TLYLLFVWLGPKWMDREPFQMLVLI IYNFGMVLLNLFIFRELLMGSYNAGYSYICQSV
sp|Q9EQC4.2|ELO -----EPFQMLVLI IYNFGMVLLNLFIFRELFMGSYNAGYSYICQSV
XP_032765767.1 TLYLLFVWLGPKWMDREPFQMLVLI IYNFGMVLLNLFIFRELFMGSYNAGYSYICQSV
XP_011363206.1 TLYLLFVWLGPKWMDREAFQMLVLI IYNFGMVLLNLFIFRELFMGSYNAGYSYICQSV
AAI42460.1 TLYLLFVWLGPKWMDREPFQMLVLI IYNFGMVLLNLFIFRELLMGSYNAGYSYICQTV
XP_007104948.1 TLYLLFVWLGPKWMDREPFQMLVLI IYNFGMVLLNLFIFRELFMGSYNAGYSYICQSV
XP_001366145.1 TLYLLFVWLGPKWMDREPFQMLVLI IYNFGMVLLNLFIFRELFLASTAAGYSYICQSV
XP_028902935.1 TLYLLFVWLGPKWMDREPFQMLVLI IYNFGMVLLNLFIFKELFLGSAAGYSYICQSV
XP_046770079.1 TIYLLTVWLGPKWMDREPFQMLVLI IYNFGMVLLNLFIFKELFLSRRARGYSYICQTV
XP_005299664.1 TLYLLTVWLGPKWMDREPFQMLVLI IYNFGMVLLNLFIFKELFLASRRARGYSYICQTV
XP_026520959.1 TLYLLAVWLGPKWMDREPFQMLVLI IYNFGMVLLNLFIFKELLLSRRARGYSYICQSV
XP_002936253.1 TAYLLVWVWLGPKFMKNREPFQMLVLI IYNFGMVLI IYNFGMVLI IYNFGMVLI IYNFGMVLI
ADJ95235.1 CLYLLFLWAGPKYMQNREPFQMLVLI IYNFMSVMI IYNFMSVMI IYNFMSVMI IYNFMSVMI
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HumanElovl5 -RTAGESDMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Macaca.NP_00130 -RTAGESDMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
SeaLion.XP_0274 -RSAGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Bat.XP_03626954 -RSAGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
FruitBat.XP_037 -RSAGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Mouse.NP_599016 -RSAGESDMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVM
Rat.NP_599209.1 -RSAGESDMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVM
Beaver.JAV42152 -RSAGESDMKI IQVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Pangolin.XP_017 -RSSGEADVIVIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHVSMMLNIWWFVM
ChPangolin.XP_0 -RSSGEADVIVIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHVSMMLNIWWFVM
Mole.XP_0373757 -RSAGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Bos.NP_00104006 -RSAGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
BlueWhale.XP_03 -RSAGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Dolphin.XP_0198 -RSAGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Gallus.NP_00118 -HSGGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVM
Duck.NP_0012973 -HSGGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVM
Falcon.XP_03724 -HSGGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVM
Turtle.XP_03775 -HSGGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Komodo.KAF72468 -HSGGEADMKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVM
Xenopus.NP_0010 -NSGGDADTKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Salmo.NP_001130 -HSAGETDTKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Pike.AFR36912.1 -RSAGEADTKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Croaker.NP_0012 -HSAQEVNKKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Rockfish.XP_037 -HSAQEVNKKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
AmSole.BBL33563 -HSAQEVNKKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Eel.XP_03525699 -HSAQEVNKKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVM
Sturgeon.XP_033 -HSGGDADTKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVM
Zebrafish.NP_95 -HSGGDADTKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVM
Eshark.XP_00789 -HSAGKADLKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVM
WhaleShark.XP_0 -HNAGEADLKI IIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVM
sp|Q9GZR5.1|ELO DYSNDVNEVRIAAALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
XP_008683076.1 DYSNDVNEVRIAAALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
XP_002714591.1 DYSNDVNEVRIAAALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
sp|Q9EQC4.2|ELO DYSNDVNEVRIAGALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
XP_032765767.1 DYSNDVNEVRIAAALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
XP_011363206.1 DYSNDVNEVRIAAALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
AAI42460.1 DYSNDVNEVRIAAALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
XP_007104948.1 DYSNDVNEVRIAAALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
XP_001366145.1 NYSDDVNEVRIAGALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
XP_028902935.1 DYSNDVNEVRIAAALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
XP_046770079.1 DYSNDVNEVRIAAALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
XP_005299664.1 DYSNDVNEVRIAGALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
XP_026520959.1 DYSNDVNEVRIAGALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
XP_002936253.1 DYSDDENEVRIASALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
ADJ95235.1 SYSNDVNEVRIASALWYFVSKGVEYLDTVFFILRKNNHQITVLHVYHHCTMFTLWVIGI
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HumanElovl5 NWWPCGHSYFGATLNSFIHVMYSYGLSSV-PSMRPYLWKKYITQGQLLQVLTIIQT

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Macaca.NP_00130 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSV-PSMRPYLWKKYITQGQLLQFVLTIIQT
SeaLion.XP_0274 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSV-PSVPRPYLWKKYITQGQLLQFVLTIIQT
Bat.XP_03626954 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSV-PSMRPYLWKKYITQGQLI QFVLTIIQT
FruitBat.XP_037 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSV-PSMRPYLWKKYITQGQLLQFVLTIVQT
Mouse.NP_599016 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSI-PSMRPYLWKKYITQGQLVQFVLTIIQT
Rat.NP_599209.1 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSV-PSMRPYLWKKYITQGQLVQFVLTIIQT
Beaver.JAV42152 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSV-PSMRPYLWKKYITQGQLI QFVLTIIQT
Pangolin.XP_017 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSV-PSMRPYLWKKYITQGQLLQFVLTIIQT
ChPangolin.XP_0 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSV-PSMRPYLWKKYITQGQLLQFVLTIIQT
Mole.XP_0373757 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSV-PSMRPYLWKKYITQGQLLQFVLTIIQT
Bos.NP_00104006 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSI-PSMRPYLWKKYITQGQLLQFVLTIIQT
BlueWhale.XP_03 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSV-PSMRPYLWKKYITQGQLLQFVLTIIQT
Dolphin.XP_0198 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSSV-PSMRPYLWKKYITQGQLVQFVLTIIQT
Gallus.NP_00118 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSAV-PAMRPYLWKKYITQGQLI QFVLTIFQT
Duck.NP_0012973 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSAV-PAMRPYLWKKYITQGQLTQFVLTIFQT
Falcon.XP_03724 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSAV-PAMRPYLWKKYITQGQLI QFVLTIFQT
Turtle.XP_03775 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSAI-PAMRPYLWKKYITQGQLI QFVLTIFQT
Komodo.KAF72468 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSAI-PSMRPYLWKKYITQGQLI QFVLTIFQT
Xenopus.NP_0010 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSAI-PAMRPYLWKKYITQCLTQFVLTMTQT
Salmo.NP_001130 NWVPCGHSYFGATLNSFVHVLMSYSGYGLSAV-PAIRPYLWKKYITQGQLI QFVLTMSQT
Pike.AFR36912.1 NWVPCGHCYFGACLNSFIHVLMSYSGYGLSAI-PTMRPYLWKKYITQGQLI QFVLTMTQT
Croaker.NP_0012 NWVPCGHSYFGASLNSFVHVMYSYGLSAI-PAMRPYLWKKYITQLQTLQFVLTMSQT
Rockfish.XP_037 NWVPCGHSYFGASLNSFVHVMYSYGLSAI-PAIRPYLWKKYITQFQLI QFVLTMSQT
AmSole.BBL33563 NWVPCGHSYFGASLNSFVHVMYSYGLSAI-PAMRPYLWKKYITQLQTLQFVLTMSQT
Eel.XP_03525699 NWVPCGHSYFGASLNSFIHVLMSYSGYGLSAV-PALRPYLWKKYITQGQLI QFVMTMIQT
Sturgeon.XP_033 NWVPCGHSYFGASLNSFIHVLMSYSGYGLSAI-PAVRPYLWKKYITQGQLI QFVLTMSQT
Zebrafish.NP_95 NWVPCGHSYFGATFNSFIHVLMSYSGYGLSAV-PALRPYLWKKYITQGQLVQFVLTMSQT
Eshark.XP_00789 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSAI-PAMRPYLWKKYITQGQLI QFVMTIIQT
WhaleShark.XP_0 NWVPCGHSYFGATLNSFIHVLMSYSGYGLSAI-PAMRPYLWKKYITQGQLI QFVLTIIQT
sp|Q9GZR5.1|ELO KVVAGGQAFFGAQLNSFIHVMYSYGLTAFGPWIQKYLWKKRYLTMLQLI QFHVLTIGHT
XP_008683076.1 KVVAGGQAFFGAQLNSFIHVMYSYGLTAFGPWIQKYLWKKRYLTMLQLI QFHVLTIGHT
XP_002714591.1 KVVAGGQAFFGAQMNNSFIHVMYSYGLTAFGPWIQKYLWKKRYLTMLQLVQFHVLTIGHT
sp|Q9EQC4.2|ELO KVVAGGQAFFGAQMNNSFIHVMYSYGLTAFGPWIQKYLWKKRYLTMLQLVQFHVLTIGHT
XP_032765767.1 KVVAGGQAFFGAQMNNSFIHVMYSYGLTAFGPWIQKYLWKKRYLTMLQLVQFHVLTIGHT
XP_011363206.1 KVVAGGQAFFGAQLNSFIHVMYSYGLTAFGPWIQKYLWKKRYLTMLQLVQFVVTIGHT
AAI42460.1 KVVAGGQAFFGAQMNNSFIHVMYSYGLTAFGPWIQKYLWKKRYLTMLQLVQFHVLTIGHT
XP_007104948.1 KVVAGGQAFFGAQMNNSFIHVMYSYGLTAFGPWIQKYLWKKRYLTMLQLVQFHVLTIGHT
XP_001366145.1 KVVAGGQAFFGAQLNSFIHVMYSYGLTAFGPWIQKYLWKKRYLTMLQLVQFVVTIGHT
XP_028902935.1 KVVAGGQAFFGAQLNSFIHVMYSYGLAALGPKQKYLWKKRYLTMLQLVQFHVLTIGHT
XP_046770079.1 KVVAGGQAFFGAQMNNSFIHVMYSYGLAALGPKQKYLWKKRYLTMLQLVQFHVLTIGHT
XP_005299664.1 KVVAGGQAFFGAQMNNSFIHVMYSYGLAALGPKQKYLWKKRYLTMLQLVQFHVLTIGHT
XP_026520959.1 KVVAGGQAFFGAHINALIHVMYSYGLAALGPKQKYLWKKRYLTMLQLVQFHVLTIGHT
XP_002936253.1 KVVAGGQAFFGAHINALIHVMYSYGLAALGPKQKYLWKKRYLTMLQLVQFHVLTIGHT
ADJ95235.1 KVVAGGQAFFGAGINSSIHVMYSYGLAALGPKQKYLWKKRYLTMLQLVQFHVLTIGHT
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HumanElovl5 SCGVIWPCFPLGWL YFQIGYMSLIALFTNFYIQTYNKKGAS-----RRKDHLKDHQ
Macaca.NP_00130 SCGVIWPCFPLGWL YFQIGYMSLIALFTNFYIQTYNKKGAS-----RRKDHLKDHQ
SeaLion.XP_0274 SCGVIWPCFPLGWL YFQIGYMSLITLFTNFYVQTYNKKGAS-----RRKEHLKDHQ
Bat.XP_03626954 TCGVIWPCSFPLGWL YFQIGYMSLITLFTNFYIQTYNKQGAS-----RRKEHLKDHQ
FruitBat.XP_037 SCGVIWPCSFPLGWL YFQIGYMSLITLFTNFYIQTYNKKGAS-----RRKERLRDHQ
Mouse.NP_599016 TCGVWPCSFPLGWL YFQIGYMSLIALFTNFYIQTYNKKGAS-----RRKDHLKGHQ
Rat.NP_599209.1 SCGVIWPCSFPLGWL YFQIGYMSLIALFTNFYIQTYNKKGAS-----RRKEHLKGHQ
Beaver.JAV42152 SCGVIWPCSFPLGWL YFQIGYMSLIALFTNFYIQTYNKKGAS-----RRRDHLKDHQ
Pangolin.XP_017 SCGVIWPCFPLGWL YFQIGYMSLIVLFTNFYVQTYNKKGAS-----RRREYLKDHQ
ChPangolin.XP_0 SCGVIWPCAFPLGWL YFQIGYMSLIVLFTNFYVQTYNKKGAS-----RRREYLKDHQ
Mole.XP_0373757 TCGVIWPCFPLGWL YFQIGYMSLITLFTNFYIQTYNKKGAS-----RRKEHLKDHQ
Bos.NP_00104006 SCGVIWPCFPLGWL YFQIGYMSLITLFTNFYIQTYNKKGVS-----RRREHQKDHQ
BlueWhale.XP_03 SCGVIWPCAFPLGWL YFQIGYMSLIALFTNFYIQTYNKKGAS-----RRREHQKDHQ
Dolphin.XP_0198 SCGVIWPCAFPLGWL YFQIGYMSLIALFTNFYIQTYNKKGAS-----RRRE----HQ
Gallus.NP_00118 SCGVIWPCAFPLGWL YFQIFYMSLITLFTNFYIQTYNKKASS-----RRKE----YQ
Duck.NP_0012973 SCGVIWPCAFPLGWL YFQISYMSLITLFTNFYIQTYNKKASS-----RRKE----YQ
Falcon.XP_03724 SCGVIWPCAFPLGWL YFQISYMSLITLFTNFYIQTYNKKASS-----RRKE----YQ
Turtle.XP_03775 SCGVIWPCAFPLGWL YFQIFYMSLITLFTNFYIQTYNKKASS-----RRKE----YQ
Komodo.KAF72468 SCGVIWPCFPLGWL YFQIGYMITLITLFTNFYIQTYNKKAAC-----RRKE----YQ
Xenopus.NP_0010 TCAMIWPCFPLGWL YFQNCYMSLITLFTNFYIQTYNKKTSS-----RRKE----YQ
Salmo.NP_001130 ICAMIWPCFPLGWL YFQIFYMASLIAFFSNFYIQTYNKHSVS-----QKEY----HQ
Pike.AFR36912.1 ICAMIWPCFPLGWL YFQISYMTLIALFSNFYIQTYNKHSVS-----QKKEC---HR
Croaker.NP_0012 LCAMIWPCFPLGWL YFQISYMTLIFLFSNFYVQTYKHSVS-----LKKE----HQ
Rockfish.XP_037 MCAMIWPCFPLGWL YFQISYMTLIFLFSNFYIQTYNKHSVS-----LKKE----HQ
AmSole.BBL33563 MCAMIWPCFPLGWL YFQISYMTLIFLFSNFYIQTYNKHSVS-----LQKD----HR
Eel.XP_03525699 MCAMIWPCFPLGWL YFQISYMTLIALFSNFYIQTYNKHSVS-----RRKE----HQ
Sturgeon.XP_033 TCAVFRPCFPLGWL YFQICYLIVLIVLFSNFYIQTYNKHSVS-----RRKE----CQ

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

```
Zebrafish.NP_95      SCAVVWPCGPFPMGWLYFQISYMTLILLFSNFYIQTYKKRSGS-----RKSD----YP
Eshark.XP_00789    SFGVWVPCGFPSSGWLYFQIGYMISLIVLFTNFYIQTYQKKSAS-----RTKD----CL
WhaleShark.XP_0    SFGVIWPCGFPSSGWLYFQIGYMISLIIILFTNFYIQTYKKKSASF-----KSKD----CL
Human ELOVL4      ALSLYTDCPFPKMMHWALIAYAISFIFLFLNFYIRTYKEPKKP-----KAGKT----AM
XP_008683076.1    ALSLYTDCPFPKMMHWALIAYAISFIFLFLNFYVRYTYKEPKKA-----KTGKT----AV
XP_002714591.1    ALSLYTDCPFPKMMHWALIAYAISFIFLFLNFYIRTYNEPKKP-----KTGKT----AM
sp|Q9EQC4.2|ELO   ALSLYTDCPFPKMMHWALIAYAISFIFLFLNFYTRTYNEPKQS-----KTGKT----AT
XP_032765767.1    ALSLYTDCPFPKMMHWALIAYAISFIFLFLNFYTRTYNEPKKS-----KTGKT----AT
XP_011363206.1    ALSLYTDCPFPKMMHWALIAYAISFIFLFLNFYVRYTYNEPKKS-----KTGKT----AV
AAI42460.1        ALSLYTDCPFPKMMHWALIVYAVSFISFIFLFLNFYVRYTYKEPKKA-----KPGKT----AT
XP_007104948.1    ALSLYTDCPFPKMMHWALIAYAVSFISFIFLFLNFYVRYTYKEPKKA-----KPGKT----AA
XP_001366145.1    ALSLYTDCPFPKMMHWALIVYAVSFISFIFLFLNFYQTYNDPKTS-----KNRTA----AA
XP_028902935.1    AMSLYTNCPPFRMMHWALIVYAVSFISFIFLFLNFYQTYNQPKRSA-----KTGKT----AV
XP_046770079.1    ALSIYIDCPFPMMHWGVIFYAITFISFLFGNFYRTYKLPKEP-----VKNGK----IA
XP_005299664.1    AMSIYIDCPFPMMHWGVIFYAITFISFLFGNFYRTYKMPKEP-----IKNGK----IL
XP_026520959.1    ALSIYIDCPFPMMHWGVIFYAASFIVLFGNFYRTYKMPKQPKELKQEKNGK----IT
XP_002936253.1    ALSLYIDCPFPMMHWALIVYAVSFISFLFGNFYRTYKMPKQPKELKQEKNGK----LI
ADJ95235.1        GHSLYTGCFPPAWMQWALIGYAVTFISILFGNFYQTYRRTRPSA-----HKVAKP----VT
      .:  *  *  *      *      .: * : * * * * : : *
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HumanElov15      NGSMAAVNG-----HTNS-FSPLENN-----VKPRKLRKD--
Macaca.NP_00130   NGSVAAVNG-----HTNS-FSPLENN-----VKPRKLRKD--
SeaLion.XP_0274   NGSVAAVNG-----HTNS-F-SLENN-----VKPRKQRKD--
Bat.XP_03626954  NGSLTAANG-----HTNS-FSSLENN-----VKLRKQRKD--
FruitBat.XP_037  NGSVTAANG-----HTNS-FSSLGNS-----TKPRKQRKD--
Mouse.NP_599016  NGSVAAVNG-----HTNS-FPSLENS-----VKPRKQRKD--
Rat.NP_599209.1  NGSMTAVNG-----HTNN-FASLENS-----VTSRKQRKD--
Beaver.JAV42152  NGSATVVNG-----HTNT-FSSLENN-----VKPRKQRKD--
Pangolin.XP_017  NGSMAAMNG-----HAGS-FSSLGSS-----AKPRKLRKD--
ChPangolin.XP_0  NGSMAAVNG-----HAGS-FSSLGNS-----VKPRKLRKD--
Mole.XP_0373757  NGSVAAVNG-----HTNS-FSTLENN-----VKLRKQRKD--
Bos.NP_00104006  NGSVAAVNG-----HISS-FSSLENN-----VKPRKQRKD--
BlueWhale.XP_03  NGSVTAVNG-----HTSS-FSSLENN-----VKPRKQRKD--
Dolphin.XP_0198  NGSVTAVNG-----HTSS-FSSLEHS-----VKPRKQRKD--
Gallus.NP_00118  NGSTATVNG-----YTNS-FSSLENN-----VKQRKQRKD--
Duck.NP_0012973  NGSAATVNG-----YTNS-FSSLENN-----VKQRKQRKD--
Falcon.XP_03724  NGSTATVNG-----YTNS-SSSLENN-----VKQRKQRKD--
Turtle.XP_03775  NGSTAAVNG-----YTNS-FSSLENN-----VKQRKQRKD--
Komodo.KAF72468  NGSTAAVNG-----YTNS-FSSLENN-----VKQRKQRKD--
Xenopus.NP_0010  NGSASAVNG-----HTNS-FSSLEDN-----VKQRKQRQD--
Salmo.NP_001130  NGSVDSLNG-----HANG-VTPTE-T-----ITHRKVRVD--
Pike.AFR36912.1  NGSASPLNG-----HVSG-VTPIE-T-----ITHKVRAD--
Croaker.NP_0012  NGSPVSTNG-----HANG-TPSLE-H-----AAHKKLRVD--
Rockfish.XP_037  NGSPISTNG-----HANG-TPSME-R-----TAYQKLRMD--
AmSole.BBL33563  NGSPASRNG-----HANG-KPSAE-Q-----PAHKKLRVD--
Eel.XP_03525699  NGSAAAMNG-----HSNG-VSPA-E-D-----LTRRKLKRV--
Sturgeon.XP_033  NGSAAASLNG-----HANG-VSSVD-N-----VTQRKLRKD--
Zebrafish.NP_95  NGS---VNG-----HTNG-VMSSE-K-----IKHRKARAD--
Eshark.XP_00789  NGS---ANG-----HTNG-FSAQTDH-----YSAKKTTH---
WhaleShark.XP_0  NGSTIAANG-----HTNG-LSTQMDH-----YSEKKTTH---
sp|Q9GZR5.1|ELO  NGI--SANG-----VSKSEKQLMIENG--KKQKNGKAKGD
XP_008683076.1   NGI--SANG-----VSKSEKQLVIENG--KKQKNGKAKGE
XP_002714591.1   NGI--SANG-----VSKSDNQLVIENG--KKQKNGKAKGE
sp|Q9EQC4.2|ELO  NGI--SSNG-----VSKSEKAL--ENG--KPQKNGKPKGE
XP_032765767.1  NGI--SANG-----VSKSEKQLVLENG--KPQKNGKPKGE
XP_011363206.1  NGI--SANG-----VSKSEK-LVMENG--KKQKNGKAKGE
AAI42460.1       NGI--SANG-----VSKSENHLVVENG--KKQKNGKAKGE
XP_007104948.1  NGI--SANG-----VNQSENHLVVENG--KKQKNGKAKRE
XP_001366145.1  NGI--SANG-----ISKSEKQLVMENG--KKKHNGKAKGE
XP_028902935.1  NGI--TTNG-----VSKSESQSVVENG--KKKNGKAKGE
XP_046770079.1  NGA--VANG-----VSKPENNPVVENG--KKQKNGKAKGE
XP_005299664.1  NGA--VANG-----VSKLENNLVVENG--KKQKKEKAKGE
XP_026520959.1  NGV--IANG-----KSKPENGAVMENG--KVQKK--AKGE
XP_002936253.1  NGK-TSVNGKSSVNGKCQINGKLMNGAVNGAVSKQDNKVGQENG--RKRKGRKAKRE
ADJ95235.1       NGVSMATNG-----YNKLQD--VEENGLKQKKGRKAKRE
      **      **      :
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Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

Supplementary Table 10 MSA of ELOVL5 (7 sequences) + ELOVL2 (7 sequences) + ELOVL4 (7 sequences)

CLUSTAL format alignment by MAFFT (v7.505); L-INS-I method; Blosum 62 matrix.

```
human_ELOVL5 -----MEHFDASLSTYFKALLGPRDTRVKGWFLLDNYIPTFVCSVIYLLIV
mus_ELOVL5 -----MEHFDASLSTYFKAFGLGPRDTRVKGWFLLDNYIPTFVCSVIYLLIV
rat_ELOVL5 -----MEHFDASLSTYFRALLGPRDTRVKGWFLLDNYIPTFVCSAIYLLIV
bos_ELOVL5 -----MEHFDASLSTYFRAWLGPRDTRVEGWFLLDNYVPTLVCSILYLLIV
gallus_ELOVL5 -----MERLDKTINSYLDVWLGPRDPRVKGWLLLENYPTTFIFSVLYLLIV
frog_ELOVL5 -----MEVLDKAVNGYIDHLLGPKDPRVKGWLLLDNYVPTIFFTALYLFIV
salmo_ELOVL5 -----MEAFNHKLNTYIDSWMGPRDERVQGWLLLDNYPPFTALTMYYLLIV
human_ELOVL2 -----MEHLKAFDDEINAFLDNMFGRDSDRVRGWFMLDSYLPFTFLLTVMYLLSI
bos_ELOVL2 -----MEHLKAFDDEVNAFLDNMFGPRDSDRVRGWFMLDSYLPFTFLLTIVYLLSI
mus_ELOVL2 -----MEQLKAFDNEVNAFLDNMFGPRDSDRVRGWFLLDSYLPFTILTITYLLSI
rat_ELOVL2 -----MEQLKAFDNEVNAFLDNMFGPRDSDRVRGWFLLDSYLPFTLTIVYLLSI
gallus_ELOVL2 -----MEHLKAFDQEVNAFVDYMFGRDARVRGWLLDSYLPFTFLLTVAYLLCI
frog_ELOVL2 -----MEHIEKLDQEVNAFVDYLFGRDTRVRGWMLDSYLPFTFLLTLLYLLSI
salmo_ELOVL2 -----MNHQLSLDERLNKLFYFLFEDRSDRVRGWLLDSYLPFTLSLTILYLLSV
human_ELOVL4 MGLLDSEPGSVLNVSTALNDTVEFYRWTWSIADKRVENWPLMQSPWPPTSISTLYLLFV
mus_ELOVL4 MGLLDSEPGSVLNAVSTAFNDTVEFYRWTWSIADKRVEDWPLMQSPWPPTSISTLYLLFV
rat_ELOVL4 MGLLDSEPGSVLNAVSTAFNDTVEFYRWTWSIADKRVEDWPLMQSPWPPTSISTLYLLFV
bos_ELOVL4 MGLLDSEPGSVLNAVSTALNDTVEFYRWTLSITDKRVENWPLMQSPLPTLCISTLYLLFV
gallus_ELOVL4 MGA AAAEPPRAAGLVSVLNDTLEFYRWTWSIRDKRVDWPLMQSPPTLTISTIYLLTV
frog_ELOVL4 -----MLNPVSDVIQRTLRLYDWCLSIDDKRVEKWPLMQSPLPTLAISTVYLLV
salmo_ELOVL4 -----MELTTHLINDTMNLYKWALTADKRVEKWPLMDNPLPTLAISSSYLLFL
* * * * : : : : * * * * :
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```
human_ELOVL5 WLGPKYMRNKQPFSCRGILVVYNLGLTLLSLYMFCELVTVGWEGKYNFFCQGTR-TAGES
mus_ELOVL5 WLGPKYMKNRQPFSCRGILQLYNLGLTLLSLYMFYELVTGVWEGKYNFFCQGTR-SAGES
rat_ELOVL5 WLGPKYMKNRQPFSCRGILVVYNLGLTLLSLYMFYELVTGVWEGKYNFFCQGTR-SAGES
bos_ELOVL5 WLGPKYMKTRQPFSCRGILVVYNLGLTLLSLYMFCELVTVGWEGQYNFFCQGTR-SGGEA
gallus_ELOVL5 WLGPKYMRNKQPFSCRGILVVYNLGLTLLSLYMFYELVTGVWEGGYNFYCQDTH-SGGEA
frog_ELOVL5 WRGPKYMQNRQPFVSCRSILVVYNLGLTLLSFYMFYELVTGVWEGGYNFFCQDTH-SGGDA
salmo_ELOVL5 WLGPKYMRHRQPFVSCQGLLVLYNLALTLLSFYMFYEMVSAVWQGGYNFYCQDTH-SAGET
human_ELOVL2 WLGNYMKNRPALSLRGIILTLYNLGITLLSAYMLAELIISTWEGGYNLQCQDLT-SAGEA
bos_ELOVL2 WLGNYMKNRPALSLRGIILTLYNLGITLLSAYMLAELIISTWEGGYNLQCQDLT-SAGEA
mus_ELOVL2 WLGNYMKNRPALSLRGIILTLYNLGITLLSAYMLVLELISWEGGYNLQCQNLND-SAGEG
rat_ELOVL2 WLGNYMKNRPALSLRGIILTLYNLGITLLSAYMLVLELISWEGGYNLQCQNLND-SAGEG
gallus_ELOVL2 WLGPKYMKNRQPFSLKAHLIVYNLGLTLLSLYMLIELIATWEGGYNLQCQNLH-SAGEA
frog_ELOVL2 WLGPKYMKDRPAFSLRGHLIVYNLGLTLLSFYMLIELIISTWQGAYNLQCQNLND-SAGEA
salmo_ELOVL2 YLGSKYMRNRPAFSLKGVLVQVNFVSTMLSLYMLVLELISATLSAGYRLQCQGLH-EAGEA
human_ELOVL4 WLGPKWMDREPFQMRVLVLIYVNFVGMVLLNLFIFRELFMGSYNAGYSYICQSVSDYSNNVH
mus_ELOVL4 WLGPKWMDREPFQMRVLVLIYVNFVGMVLLNLFIFRELFMGSYNAGYSYICQSVSDYSNDVN
rat_ELOVL4 WLGPKWMDREPFQMRVLVLIYVNFVGMVLLNLFIFRELFMGSYNAGYSYICQSVSDYSNDVN
bos_ELOVL4 WLGPKWMDREPFQMRVLVLIYVNFVGMVLLNLFIFRELFMGSYNAGYSYICQTVSDYSNDVH
gallus_ELOVL4 WLGPKWMDREPFQMRVLVLIYVNFVGMVLLNLFIFRELFMGSYNAGYSYICQTVSDYSNDVY
frog_ELOVL4 WLGPFVFMKNREPFRLRYLLIAYNFGMVLNLFIFKELFLGAKAAGYSYICQTVSDYSDDEN
salmo_ELOVL4 WLGPKYMQNREPFQKTLIVYVNFVSMVIFNFFICKELFLAARAAGYSYICQSVSDYSDDPN
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human_ELOVL5 DMKIIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVMMNWVPCGH
mus_ELOVL5 DMKIIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVMMNWVPCGH
rat_ELOVL5 DMKIIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVMMNWVPCGH
bos_ELOVL5 DMKIIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVMMNWVPCGH
gallus_ELOVL5 DMKIIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHATMLNIWWFVMMNWVPCGH
frog_ELOVL5 DTKIIRVLWYYYFSKLIIEFMDTFFFILRKNNHQITVLHVYHHASMLNIWWFVMMNWVPCGH
salmo_ELOVL5 DTKIINVLWYYYFSKVIIEFMDTFFFILRKNNHQITFLHVIYHHASMLNIWWFVMMNWVPCGH
human_ELOVL2 DIRVAKVLWYYYFSKSVIEFLDTIFFVLRKKTSSQITFLHVYHHASMFNIWWCVLNIWPCGQ
bos_ELOVL2 DIRVAKVLWYYYFSKLIIEFLDTIFFVLRKKTSSQITFLHVYHHASMFNIWWCVLNIWPCGQ
mus_ELOVL2 DVRVAKVLWYYYFSKLVIEFLDTIFFVLRKKTSSQITFLHVYHHASMFNIWWCVLNIWPCGQ
rat_ELOVL2 DIRVAKVLWYYYFSKLVIEFLDTIFFVLRKKTSSQITFLHVYHHASMFNIWWCVLNIWPCGQ
gallus_ELOVL2 DIRVAKVLWYYYFSKVIIEFADTIFVLRKKTSSQITFLHVYHHATMFNIWWCVLNIWPCGQ
frog_ELOVL2 DVRVAKVLWYYYFSKAIIEFMDTIFVLRKKTSSQITFLHVYHHATMFNIWWCVLNIWPCGQ
salmo_ELOVL2 DLRVAKVLWYYYFSKVIIEFLDTIFFVLRKKTSSQITFLHVYHHASMFNIWWCVLNIWPCGQ
human_ELOVL4 EVRIAAALWYFVSKGVEYLDTVFFILRKNNHQVSLHVYHHCTMFTLWVIGIKWVAGGQ
mus_ELOVL4 EVRIAGALWYFVSKGVEYLDTVFFILRKNNHQVSLHVYHHCTMFTLWVIGIKWVAGGQ
```

Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

```
rat_ELOVL4      EVRIAAALWVYFVSKGVEYLDTVFFILRKKNNQVVSFLHVVHCTMFTLWWIGIKWVAGGQ
bos_ELOVL4      EVRIAAALWVYFISKGIEYLDTVFFILRKKNNQVVSFLHVVHCTMFTLWWIGIKWVAGGQ
gallus_ELOVL4   EVRIAAALWVYVSKGIEYLDTVFFILRKKFNQISFLHVVHCTMFTLWWIGIKWVAGGQ
frog_ELOVL4     EVRVASALWVYVSKGVEYFDTVFFILRKKFNQISFLHVVHCTMFTLWWIGIKWVAGGQ
salmo_ELOVL4    EVRIAAALWVYFISKGVEYLDTVFFILRKKFNQVVSFLHVVHCTMFTLWWIGIKWVAGGQ
: : : .****:.* * : * : **.*:*** : * : .**:* ** : * : . * :
: : : .****:.* * : * : **.*:*** : * : .**:* ** : * : . * :

human_ELOVL5    SYFGATLNSFIHVLMSYYGLSSV-PSMRPYLWKKYITQGQLLQFVLTIIQTSCGVIWP
mus_ELOV5       SYFGATLNSFIHVLMSYYGLSSI-PSMRPYLWKKYITQGQLVQFVLTIIQTTCGVFWP
rat_ELOVL5      SYFGATLNSFIHVLMSYYGLSSV-PSMRPYLWKKYITQGQLVQFVLTIIQTSCGVIWP
bos_ELOVL5      SYFGATLNSFIHVLMSYYGLSSV-PSMRPYLWKKYITQGQLVQFVLTIIQTSCGVIWP
gallus_ELOVL5   SYFGATLNSFIHVLMSYYGLSAV-PAIRPYLWKKYITQGQLIQFVLTIFQTSAGVWP
frog_ELOVL5     SFFGATLNSFIHVLMSYYGLSAI-PAIRPYLWKKYITQCQLTQFVLTMTQTTCAMIWP
salmo_ELOVL5    SYFGASLNSFVHVLMSYYGLSAV-PAIRPYLWKKYITQGQLIQFVLTMSQTICAVIWP
human_ELOVL2    SFFGPTLNSFIHILMSYYGLSVF-PSMHKYLWKKYLTQAQLVQFVLTITHTMSAVVKP
bos_ELOVL2      SFFGPTLNSFIHILMSYYGLSVF-PSMHKYLWKKYLTQAQLVQFVLTITHTMSAVVRP
mus_ELOVL2      SFFGPTLNSFIHILMSYYGLSVF-PSMHKYLWKKYLTQAQLVQFVLTITHTLSAVVKP
rat_ELOVL2      SFFGPTLNSFIHILMSYYGLSVF-PSMHRYLWKKYLTQAQLVQFVLTITHTLSAVVKP
gallus_ELOVL2   SFFGPTLNSFIHVLMSYYGLSVI-PSMRKYLWKKYLTQAQLIQFVLTIVHTLSAAVKP
frog_ELOVL2     SFFGPTLNSFIHVLMSYYGLSVI-PSMHKYLWKKYLTQAQLVQFVLTITHTLSAAVKP
salmo_ELOVL2    SFFGPTLNSFIHVCMSYYGLSTI-PSMQKYLWKKRYLTQAQLIQFILTITHTLSAIVVP
human_ELOVL4    AFFGAQLNSFIHVIMSYYGTLAFGPWIQKYLWKKRYLTMLQLIQFHVITIGHTALSLYTD
mus_ELOVL4      AFFGAQMNSFIHVIMSYYGTLAFGPWIQKYLWKKRYLTMLQLVQFHVITIGHTALSLYTD
rat_ELOVL4      AFFGAQMNSFIHVIMSYYGTLAFGPWIQKYLWKKRYLTMLQLVQFHVITIGHTALSLYTD
bos_ELOVL4      AFFGAQLNSFIHVIMSYYGTLAFGPWIQKYLWKKRYLTMLQLVQFHVITIGHTALSLYTD
gallus_ELOVL4   AFFGAQMNAFIHVIMMYGTLAACGPKVQKYLWKKRYLTILQLVQFHVITIGHTALSIIYD
frog_ELOVL4     SFFGAHMNALIHVVMYLYYGLAACGPHLQKYLWKKRYLTILQLVQFHVITIGHTALSIIYD
salmo_ELOVL4    SFFGAHMNAIHLVLMYLYYGLASFGPKIQKYLWKKRYLTIVIQMVQFHVITIGHTALSIIYD
: : * . : * : : * : * * : * : * : * : * : * : * : * : * : * : * :

human_ELOVL5    CTFPLGWLFFQIGYMISLIALFTNFYIQT---NKKGASRRKDHLDKDHQNGSMAAVNGH
mus_ELOV5       CSFPLGWLFFQIGYMISLIALFTNFYIQT---NKKGASRRKDHLDKDHQNGSVAAVNGH
rat_ELOVL5      CSFPLGWLFFQIGYMISLIALFTNFYIQT---NKKGASRRKEHLKDHQNGSMTAVNGH
bos_ELOVL5      CTFPLGWLFFQIGYMISLITLFTNFYIQT---NKKGVSRREHDKDHQNGSVAAVNGH
gallus_ELOVL5   CAFPGWLFFQIFYMISLILFTNFYIQT---NKKASSRKE---YQNGSTATVNGY
frog_ELOVL5     CKFPMGWLFFQNSYMISLILFTNFYIQT---NKKTSRREHDKDHQNGSVAAVNGY
salmo_ELOVL5    CGFPRGWLFFQIFYMASLIAFFSNFYIQT---KKHRVSQKEY---HQNGSVDSLNGH
human_ELOVL2    CGFPFGCLIFQSSYMLTLVILFVNFYIQT---RKKPMKKDMQ---EPPAGKEVKNGF
bos_ELOVL2      CGFPFGCLIFQSSYMLTLVILFVNFYIQT---RKKPMKKAME---E--AGKEVKNGF
mus_ELOVL2      CGFPFGCLIFQSSYMLTLVILFVNFYIQT---RKKPVKKELO---E---KEVKNGF
rat_ELOVL2      CGFPFGCLIFQSSYMLTLVILFVNFYIQT---RKKPMKKEMP---EGAAGKEVKNGF
gallus_ELOVL2   CGFPFGCLMFQSSYMATLVILFVNFYIQT---QKAPSRATAK---ETPVTTEVKNGY
frog_ELOVL2     CGFPFGCLMFQSSYMTLVILFVNFYIQT---KKRPSKSDPN---GIPVLTEMKNGY
salmo_ELOVL2    CGFPFGCLLFQFSYMATLVILFVNFYIQT---RKRREEE---SIKSSR
human_ELOVL4    CPFPKMHWALIAAISFIFLFNFYIRTY---KEPKKPKAGKT---AMNGISA--NGV
mus_ELOVL4      CPFPKMHWALIAAISFIFLFNFYIRTY---NEPKQSKTGKT---ATNGISS--NGV
rat_ELOVL4      CPFPKMHWALIAAISFIFLFNFYIRTY---NEPKKSKTGKT---ATNGISA--NGV
bos_ELOVL4      CPFPKMHWALIVYAVSFIFLFNFYVRTY---KEPKKAKPGKT---ATNGISA--NGV
gallus_ELOVL4   CPFPKMHWGVIFYAITFIFLFGNFYVRTY---KLPKEPVKNGK---IANGAVA--NGV
frog_ELOVL4     CPFPKMHWALIVYAITFIFLFGNFYVRTY---NAPKAATKSGKS---LTNGKTS-VNGK
salmo_ELOVL4    CEFPKMHYALICYALTFIALFGNFYVRTYRRTPRQPREPKASKA---LSNGVS---NGL
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human_ELOVL5    TNSFSPS-----ENNPKPRKLRK--D
mus_ELOV5       TNSFSPS-----ENSVKPRKQQRK--D
rat_ELOVL5      TNNFASL-----ENSVTSRKQQRK--D
bos_ELOVL5      ISSFSSL-----ENNPKPRKQQRK--D
gallus_ELOVL5   TNSFSSL-----ENNPKQQRKQQRK--D
frog_ELOVL5     TNSFSSL-----EDNVKQQRKQQRK--N
salmo_ELOVL5    ANGVTPT-----E-TITHRKRVRV--D
human_ELOVL2    SKAYFTA-----ANGVMNKKQAQ----
bos_ELOVL2      SKAYFST-----ANGVISKKAQ----
mus_ELOVL2      PKAHLIV-----ANGMTDKKAQ----
rat_ELOVL2      PKAHSIA-----ANGVTDKKVQ----
gallus_ELOVL2   HKNYFAA-----SNGFLSNKKAQ----
```


Spinocerebellar ataxia 38: structure-function analysis shows ELOVL5 G230V is proteotoxic, conformationally altered and a mutational hotspot

Ferrero et al.

```
frog_ELOVL2      HKDLINA-----SNGVLHKKEQ----
salmo_ELOVL2    PNGHSVS-----TNGTSFKKRK----
human_ELOVL4    SKSEKQLMI-----ENGKKQKNGKAKGD
mus_ELOVL4      NKSEKAL-----ENGKPKQKNGKPKGE
rat_ELOVL4      NKSEKQLVL-----ENGKPKQKNGKPKGE
bos_ELOVL4      NKSENHLVV-----ENGKKQKNGKAKGE
gallus_ELOVL4   SKPENNPVV-----ENGKKQKKGKAKGE
frog_ELOVL4     SSMNGKSPVNGKSMNGKSLMNGAVNGAVSKQDYKVGQENGRKRRKGRAKRE
salmo_ELOVL4    SKGLGNGAVVGGGKVEEKERSSGVDN-----GNRRRKRKGRAKRD
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