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(71) Applicants: **PRESIDENT AND FELLOWS OF HARVARD COLLEGE** [US/US]; 17 Quincy Street, Cambridge, MA 02138 (US). **OHIO STATE INNOVATION FOUNDATION** [US/US]; 1524 North High Street, Columbus, OH 43210 (US). **MASSACHUSETTS EYE AND EAR INFIRMARY** [US/US]; 243 Charles Street, Boston, MA 02114 (US).

(72) Inventors: **COREY, David, P.**; 127 Homer Street, Newton, MA 02459 (US). **INDZHYKULIAN, Artur**; C/o Massachusetts Eye And Ear Infirmary, 243 Charles Street, Boston, MA 02114 (US). **SOTOMAYOR, Marcos**; 772 Biosciences Building, 484 W. 12th Ave, Columbus, OH 43210 (US). **IVANCHENKO, Maryna, V.**; C/o Harvard University, Richard A. And Susan F. Smith Campus Center, Suite 727, 1350 Massachusetts Avenue, Cambridge, MA 02138 (US). **PETERS, Cole, W.D.**; C/o Harvard University, Richard A. And Susan F. Smith Campus Center, Suite 727, 1350 Massachusetts Avenue, Cambridge, MA 02138 (US).

(74) Agent: **GE, Lingyin** et al.; Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210-2206 (US).

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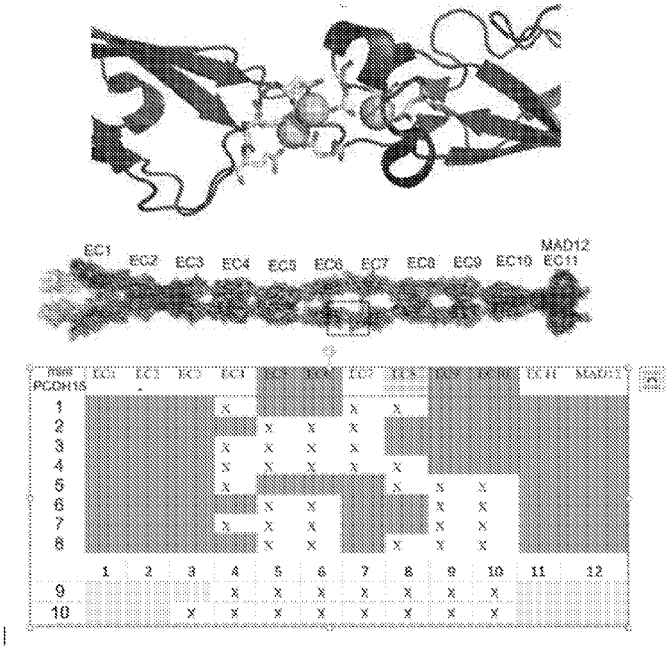


FIG. 1B

(57) Abstract: Aspects of the disclosure relate to compositions, nucleic acids, vectors, viruses, and methods useful for treating hearing loss and/or blindness, for example, Usher Syndrome type IF. The present disclosure provides isolated nucleic acids, vectors, and rAAV.9.PHP.B comprising a transgene encoding a mini-PCDH15, and methods of treating hearing loss using the same. The present disclosure also provides a gRNA associated with a base editor to correct one or more mutations in PCDH15 for treating hearing loss and/or vision loss.

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AAV VECTORS ENCODING MINI-PCDH15 AND USES THEREOF

RELATED APPLICATIONS

This application claims priority under 35 U.S.C. § 119(e) of U.S. Provisional Application, U.S.S.N. 62/839,543, filed April 26, 2019, entitled "AAV VECTORS ENCODING MINI-PCDH15 AND USES THEREOF," which is incorporated by reference herein.

FEDERALLY SPONSORED RESEARCH

This invention was made with government support under grant numbers R01-DC016932 awarded by the National Institutes of Health. The government has certain rights in the invention.

BACKGROUND

Mutations in PCDH15 cause Usher 1F, a recessive syndrome characterized by profound congenital deafness and absence of vestibular function, and progressive blindness beginning in the second decade. Because patients who lack hearing and balance rely on vision for communication and mobility, the late-onset blindness is particularly devastating.

Currently, treatment for Usher 1F is limited to cochlear implants, and there is no treatment for the related blindness. Gene addition therapy could be an attractive treatment for those with homozygous recessive mutations. However, the PCDH15 coding sequence of ~5.8 kb is too large to fit into a single AAV capsid, which is limited to ~4.7 kb of transgene.

Moreover, although conventional AAV vectors are safe and are currently used in clinical trials, none has led to efficient expression in most types of cells in the inner ear and the cells in the eye. In previous studies, AAVs transduced inner hair cells (IHCs) efficiently but not outer hair cells.

Therefore, it is of interest to develop a functional PCDH15 that would fit into a single AAV genome and an AAV serotype that can deliver a transgene to most types of cells in the inner ear and/or the cells in the eye for treatment of hearing loss and/or blindness (*e.g.*, Usher Syndrome type 1F).

SUMMARY

The present disclosure, at least in part, relates to a recombinant Adeno-associated virus (rAAV) carrying an nucleic acid sequence (e.g., AAV genome) encoding a mini-PCDH15. Aspects of the disclosure relates to the design of a mini-PCDH15 that is small enough to fit into a single AAV genome for delivery into cells of the inner ear (*e.g.*, inner hair cells, outer hair cells) across multiple species (*e.g.*, human, mouse, rat, or non-human primates), for the treatment of hereditary hearing loss, for example, Usher syndrome type 1F.

Aspects of the disclosure provides an isolated nucleic acid including: (i) a first region comprising a first adeno-associated virus (AAV) inverted terminal repeat (ITR); and (ii) a second region comprising a transgene encoding a mini-Protocadherin related 15 (mini-PCDH15). In some aspects, the disclosure provides an isolated nucleic acid comprising a transgene flanked by adeno-associated virus (AAV) inverted terminal repeats (ITRs), wherein the transgene encodes a mini-Protocadherin related 15 (mini-PCDH15).

In some embodiments, the mini-PCDH15 transgene includes a truncated extracellular portion of a full length PCDH15. The full length PCDH15 comprises an extracellular domain as set forth in amino acid sequence of SEQ ID NO: 1.

In some embodiments, the mini-PCDH15 may not comprise one or more extracellular calcium-binding domains (EC) of the full-length PCDH15. In some examples, the mini-PCDH15 does not comprise amino acid residues 719 to 820 of SEQ ID NO: 1. In addition or alternatively, the mini-PCDH15 does not comprise amino acid residues 397 to 510 of SEQ ID NO: 1. In addition or alternatively, the mini-PCDH15 does not comprise amino acid residues 821 to 927 of SEQ ID NO: 1. In addition or alternatively, the mini-PCDH15 does not comprise amino acid residues 511 to 616 of SEQ ID NO: 1. In addition or alternatively, the mini-PCDH15 does not comprises amino acid residues 617 to 718 of SEQ ID NO: 1. In addition or alternatively, the mini-PCDH15 does not comprise amino acid residues 928 to 1036 of SEQ ID NO: 1. In addition or alternatively, the mini-PCDH15 does not comprise amino acid residues 1037 to1145 of SEQ ID NO: 1. In addition or alternatively, the mini-PCDH15 does not comprise amino acid residues 266 to 397 of SEQ ID NO: 1.

In some embodiments, the mini-PCDH15 further comprises a transmembrane domain and a cytoplasmic domain. In some embodiments, the cytoplasmic domain of PCDH15 can be a splice isoform. In some embodiments, the splice isoform of PCDH15 can be CD1, CD2, or

CD3 splice isoform. In some embodiments, the splice isoform comprises a transmembrane-intracellular domain having an amino acid sequence at least 80% identical to the amino acid sequence of of SEQ ID NOs: 16, 59 or 60.In some embodiments, the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 31, 75, or 76. In some embodiments, the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 32, 77, or 78. In some embodiments, the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 33, 79, or 80. In some embodiments, the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 34, 81, or 82. In some embodiments, the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 35, 84, or 84. In some embodiments, the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 36, 85, or 86. In some embodiments, the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 37, 87, or 88. In some embodiments, the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 38, 89, or 90. In some embodiments, the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 39, 91, or 92. In some embodiments, the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 40, 93, or 94. In some embodiments, the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 41, 95, or 96. In some embodiments, the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 42, 97, or 98. In some embodiments, the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 43, 99, or 100. In some embodiments, the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 44, 101, or 102. In some embodiments, the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 45, 103, or 104. In some embodiments, the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid

sequence of SEQ ID NO: 46, 105, or 106. In some embodiments, the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 71, 107, or 108. In some embodiments, the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 72, 109, or 110. In some embodiments, the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 73, 111, or 112. In some embodiments, the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 74, 113, or 114.

In some embodiments, the transgene further comprises a promoter operably linked to the transgene encoding the mini-PCDH15. One skilled in the art would understand any promoter can be used to drive expression of the mini-PCDH15. In some examples, the promoter can be a cytomegalovirus (CMV) promoter, a hybrid cytomegalovirus (CMV) immediate-early/chicken beta-actin promoter, or chicken beta-actin promoter (CAG). In other examples, the promoter is a native promoter. Exemplary native promoters include, but are not limited to, a Methyl-CpG Binding Protein 2 (MeCP2) promoter, a Ubiquitin-C (UbiC) promoter, a Bestrophin 1 (Best1) (retina native) promoter, a human red opsin (RedO) promoter, a human rhodopsin kinase (RK) promoter, a mouse cone arrestin (CAR) promoter, a human rhodopsin (Rho) promoter, a UV opsin-specific 1 (opn1sw1) promoter, a UV opsin-specific 2 (opn1sw2) promoter, an Opsin 1, Medium Wave Sensitive 2 (opn1mw2) promoter, an opsin 1, long-wave-sensitive 1 (opn1lw1) promoter, a blue cone specific promoter (sws2), an L-opsin (opn1lw1-cxxc1) promoter, a thyroid hormone receptor β (thrb) promoter, an LIM Homeobox 1a (lhx1a) promoter, a connexin 55.5 (cx55.5) promoter, a metabotropic glutamate receptor 6b (grm6b), a glial fibrillar acidic protein (gfap) promoter, a cone transducin alpha subunit (gnat2)promoter, a connexin 52.7 (cx52.7) promoter, a connexin 52.9 (cx52.9) promoter, a heat shock cognate 70-kd protein,-like (hsp70l) promoter, a yeast transcription activator protein- (GAL4-VP16) promoter, a upstream activation sequence (UAS), a visual system homeobox 1 (vsx1) promoter, or a rhodopsin (zop) promoter. In some embodiments, the promoter is a minimal promoter. In some examples, the minimal promoter can be minimal CMV promoter, CMV584bp promoter or a Jet T promoter.

In some embodiments, the isolated nucleic acid further comprises a third region, and the third region comprises a second adeno-associated virus (AAV) inverted terminal repeat (ITR). In some embodiments, the first region and/or the third region is an AAV2 ITR.

Also provided herein are vectors comprising the isolated nucleic acid as described herein. In some embodiments, the vector is a plasmid, a viral vector (e.g., AAV vector, lentiviral vector). Also provided herein, can be a host cell comprising the isolated nucleic acid or the vector described herein.

In some embodiments, a recombinant adeno-associated virus (rAAV) includes (i) a capsid protein; and (ii) the isolated nucleic acid provided herein.

In some embodiments the capsid protein is AAV5, AAV7, AAV8 or AAV9 capsid protein, or a variant thereof. In some examples, the AAV capsid protein is AAV2.7m8 or AAV8BP2. In some examples, the AAV9 capsid variant is AAV9.PHP.B. In some examples, the capsid protein comprises an amino acid sequence at least 90% identical to amino acid sequence of SEQ ID NO: 47. In other examples, the capsid protein is exoAAV. In some examples, the exoAAV is exoAAV1 or exoAAV9. In another example, the capsid protein is Anc80.

In some embodiments, rAAV is a single-stranded AAV (ssAAV) or a self-complementary AAV (scAAV).

In some embodiments, the rAAV is capable of delivering the transgene to a mammal. In some embodiments, the mammal is a human. In other embodiments, the mammal is a non-human mammal. Exemplary non-human mammal can be mouse, rat, or non-human primate. In some embodiments, the rAAV is capable of delivering the transgene to the inner ear of retina of a mammal.

In some embodiments, the rAAV is formulated for delivery to the cochlea or the retina. Exemplary cells in cochlea can be outer hair cell (OHC), an inner hair cell (IHC), spiral ganglion neurons, stria vascularis, inner sulcus, spiral ligament, vestibular system. Exemplary cells in the eye can be photoreceptor cells, and other cells in the retina within the photoreceptor inner and outer segments (IS), outer plexiform layer (OPL), inner nuclei layer (INL), ganglion cell layer (GCL), inner plexiform layer (IPL), and retinal pigment epithelium (RPE) of the eye.

Another aspect of the present disclosure relates to a pharmaceutical composition comprising the rAAV described herein, and a pharmaceutically acceptable carrier.

Another aspect of the disclosure provides a kit for treating hearing loss and/or blindness comprising the isolated nucleic acid, the vector, or the rAAV described herein.

Aspects of the present disclosure provide a method for treating hearing loss and/or vision loss in a subject in need thereof comprising: administering to the subject an effective amount of the isolated nucleic acid, or the rAAV described herein. In some embodiments, the subject is a mammal. In some embodiments, the mammal is a human. In some embodiments, the mammal is a non-human mammal. In some embodiments, the non-human mammal is mouse, rat, or non-human primate.

In some embodiments, the subject has or is suspected of having Usher Syndrome type 1F. In some embodiments, the hearing loss and/or blindness is associated with Usher syndrome type 1F. In some embodiments, the hearing loss and/or blindness is associated with a mutation in the PCDH15 gene. In some embodiments, the mutation of PCDH15 gene is a point mutation, a missense mutation, a nonsense mutation, a deletion, an insertion, or a combination thereof. In some embodiments, the subject is human; and the mutation is one or more mutations in Table 1. In some embodiments, the subject is human; and the mutation comprises c.733C>T. In some embodiments, the mutation in the PCDH15 gene results in hearing loss and/or blindness. In some embodiments, the administration results in delivery of the isolated nucleic acid or rAAV to the ear or the eye of the subject. In some embodiments, the administration results in delivery of the isolated nucleic acid, vector, or rAAV to the cochlea or the retina of the subject. In some embodiments, the administration is via injection. In some embodiments, the injection is through round window membrane of the inner ear. In some embodiments, the administration is via subretinal or intravitreal injection to the eye.

Other aspects of the disclosure relates to a method for correcting a point mutation of PCDH15 in a target sequence including contacting the target sequence with a base editor and a guide RNA. Alternatively or in addition, the disclosure also provides a method for treating hearing loss and/or blindness in a subject in need thereof, comprising: administrating an effective amount of a base editor and a guide RNA. In some embodiments hearing loss and/or blindness is associated with Usher Syndrome type 1F. In some embodiments, the subject has or is suspected of having Usher Syndrome type 1F.

In some embodiments, the base editor comprises (i) a nucleic acid programmable DNA binding protein (napDNAbp), (ii) an adenosine deaminase capable of deaminating adenine in

deoxyribonucleic acid (DNA) and (iii) a linker between (i) and (ii). In some embodiments the nucleic acid programmable DNA binding protein (napDNAbp) is a Cas9 domain. In some embodiments, the Cas9 domain is a nuclease dead Cas9 (dCas9) or a Cas9 nickase. In some embodiments, the adenosine deaminase is derived from a bacterium. In some embodiments, the adenosine deaminase is derived from *Escherichia coli.* In some embodiments, the adenosine deaminase is derived from TadA protein of *Escherichia coli.* In some embodiments, the base editor is ABEmax.

In some embodiments the point mutation of PCDH15 is associated with Usher syndrome type 1F. In some embodiments, the point mutation in PCDH15 is a point mutation. In some embodiments, the point mutation in PCDH15 is a point mutation in Table 1. In some embodiments, the point mutation in PCDH15 is c. 733C>T.

In some embodiments, the target sequence is in the genome of the subject. In some embodiments the subject is a mammal. In some embodiments, the mammal is a human. In some embodiments, the mammal is or a non-human mammal. In some embodiments, the human patient is an infant, a child or an adult.

In some embodiments, the guide RNA comprises a nucleic sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 51.

Also provided herein is a kit for treating hearing loss and/or blindness comprising: (i) the base editor; and (ii) the guide RNA as described herein.

The details of one or more embodiments of the invention are set forth in the description below. Other features or advantages of the present invention will be apparent from the following drawing and detailed description of certain embodiments, and also from the appended claims.

BRIEF DESCRIPTION OF DRAWINGS

FIGs. 1A-1O are illustrations and pictures showing the design of mini-PCDH15 to fit into a single AAV genome, and the validation of mini-PCDH15 delivered by rAAV. FIG. 1A shows arrangement of the tip-link proteins PCDH15 and CDH23 and location at stereocilia tips. Each cadherin has multiple EC domains, strung like links in a chain. FIG. 1B shows strategy for constructing mini-PCDH15 proteins. Top panel shows atomic structure of the junction between two EC domains in PCDH15, showing calcium ions and the side chains of

calcium-binding residues. The structure of PCDH15 is well understood, enabling precise deletion of EC domains with splicing that preserves calcium binding. Middle panel shows X-ray crystal structure of the entire extracellular domain of PCDH15, solved by Sotomayor and colleagues. EC1-3 and possibly EC9-10 are involved in cis dimerization. Bottom panel shows map of deleted segments for the first eight constructs. FIG. 1C is an illustration of deletion of EC domains that results in a shorter PCDH15. FIG. 1D-1F show illustrations of 8 mini-PCDH15 constructs. FIG. 1G shows validation of Pcdh15fl/flxGfi1-Cre KO mouse and PCDH15 antibody. An antibody was raised against amino acids 80–96 of PCDH15, within EC1. Left panel shows hair bundles from WT and KO mice, with actin label and antibody to PCDH15. Bundles in the KO are disorganized, and show no antibody label at P5. Middle panel shows immunogold SEM of a hair bundle in WT and KO mice. Gold beads (white dots) showing antibody label are absent in the KO, and stereocilia have disorganized heights. Right panel shows FIB-SEM 3D reconstruction of immunogold (dots) in a WT OHC. FIG. 1H shows expression of mini-PCDH15 in CHO cells. Left panels show full-length PCDH15 is located near the membrane. Antibody label of live cells before fixation, detected with SEM immunogold (white dots), shows the N-terminal epitope is extracellular. Middle panels show a mini-PCDH15 (v5) also goes to the surface and has an extracellular N-terminus. Right panels show an untransfected control. FIG. 1I shows full length PCDH15 and mini-PCDH15s are expressed in HEK cells with reasonable efficiency, and transported to the cell membrane. FIG. 1J shows full length Pcdh15-CD1, Pcdh15-CD2 and mini-Pcdh15s transport to the cell membrane, and have EC domains positioned extracellularly as in the native protein. FIG. 1K shows cells expressing full length PCDH15-CD1, or mini-PCDH15s bind to cells expressing CDH23 as the native proteins in the hair cell. FIG. 1L is an illustration of single-molecule unbinding experimental design. FIG. 1M shows immunofluorescence and immunogold localization of mini-PCDH15s. Full-length Pcdh15-CD1, mini-Pcdh15s are transport to the cell membrane, and have EC domains positioned extracellularly as in the native protein. FIG. 1N shows SEM photomicrographs of Pcdh15fl/fl,Gfi1-Cre+ (left) and Pcdh15fl/fl,Gfi1-Cre- (right) OHCs stereocilia bundles at P1 (upper) and P5 (lower). FIG. 1O shows SEM photomicrographs of *Pcdh15fl/fl,Gfi1-Cre-* (upper) and *Pcdh15fl/fl,Gfi1-Cre+*(lower) stereocilia bundles at P6.

FIGs. 2A-2F show base editing at the PCDH15 c.733C>T locus. FIG. 2A shows the A C>T mutation creates a stop codon in the coding strand (QNLNRE•T) (SEQ ID NO: 187). The reverse complement has a G>A mutation. The base editor, guided by the reverse complement gRNA, converts the A to G. FIG. 2B shows thatABE8e displays enhanced editing of the R245X mutation. FIG. 2C shows ABE8e editing in human USH1F patient induced pluripotent stem cells. FIG. 2D shows editing efficiencies with guide varieties. FIG. 2E shows base editing at R245X site using split-intein base editors. FIG. 2F shows editing of genomic loci with intein editors.

FIGs. 3A-3E are graphs showing ssAAV9-PHP.B-CMV584bp-miniPCDH15-noWPRE-BGHpolyA in rescuing hearing loss in mice. FIG. 3A shows robust eGFP expression in both IHCs and OHCs throughout the cochlea in C57BL/6 mice at P5 using ssAAV9-PHP.B-CMV584bp-eGFP-noWPRE-BGHpolyA. FIG. 3B shows ABR results in *Pcdh15fl/fl,Myo15-Cre+* mice using ssAAV9-PHP.B-CMV584bp-miniPCDH15 v8-noWPRE-BGHpolyA. FIG. 3C shows ABR results in *Pcdh15fl/fl,Myo15-Cre+* mice using ssAAV9-PHP.B-CMV584bp-miniPCDH15 v4-noWPRE-BGHpolyA. FIGs. 3D-3E show ABR results in *Pcdh15fl/fl,Myo15-Cre+* mice using ssAAV9-PHP.B-CMV584bp-miniPCDH15 v7-noWPRE-BGHpolyA.

FIG. 4 is an image showing nano-SPD assay for PCDH15 binding to CDH23 under force. Top left shows a schematic of myosin motor and linked cadherins: myosin-X with a GFP-nanotrap binds to GFP, pulling CDH-23-GFP (bait) to the tips of filopodia. If the prey protein (PCDH-15-mCherry) interacts with the bait, both will be trafficked to the tips of filopodia. Positive controls are shown in the top panels. In the middle panel, the images show experimental groups and the results demonstrate that mini-PCDH15 version 7 was properly drawn to the tips by CDH23. The bottom panel show negative control groups, and the results indicate wild-type PCDH15 with an inactivating deafness mutation (I108N) is not drawn to the tips by CDH23. Images from left to right are: GFP-tagged CDH23 was drawn to the tips of filopodia by the myosin; mCherry-tagged control PCDH15 was drawn to the tips by CDH23; and a merged image shows co-localization.

The accompanying drawings, which are incorporated in and constitute a part of this specification, illustrate certain embodiments, and together with the written description, serve to provide non-limiting examples of certain aspects of the compositions and methods disclosed herein.

DETAILED DESCRIPTION

In some aspects, the disclosure relates to compositions, nucleic acids, viruses, uses, and methods useful for treating certain genetic diseases, for example, autosomal recessive disorders, etc. Autosomal recessive disorders are diseases that result from abnormal expression or function of both alleles of a gene. Examples of autosomal recessive disorder include, but are not limited to, hereditary hearing loss (*e.g.*, Usher syndrome Type 1F), Tay-Sachs disease, cystic fibrosis, sickle cell disease, autosomal recessive polycystic kidney disease (ARPKD), and phenylketonuria (PKU).

One aspect of the disclosure relates to delivering a functional therapeutic protein (*e.g.*, PCDH15) to the target cells (*e.g.*, inner hair cells, out hair cells and photoreceptors).

Adeno-associated virus (AAV) mediated gene therapy is one approach for the treatment of genetic diseases. Currently, treatment for Usher 1F is limited to cochlear implants, and there is no treatment for the blindness. Gene addition therapy could be an attractive treatment for those with homozygous recessive mutations. However, the PCDH15 coding sequence of ~5.8 kb is too large to fit into a single AAV capsid, which is limited to ~4.7 kb of transgene.

Moreover, although conventional AAV vectors are safe and are currently used in clinical trials, none has led to efficient expression in most types of hair cells. In previous studies, AAVs transduced inner hair cells (IHCs) efficiently but not outer hair cells.

The disclosure is based, in part, on gene therapy vectors, such as viral (*e.g.*, rAAV) vectors, comprising one or more gene fragments encoding a therapeutic gene product, such as a protein or peptide (*e.g.,* a mini-PCDH15) to the target cells (*e.g.,* inner hair cells, outer hair cells, and photoreceptors).

A gene therapy vector may be a viral vector (*e.g.*, a lentiviral vector, an adeno-associated virus vector, etc.), a plasmid, a closed-ended DNA (*e.g.*, ceDNA), etc. In some embodiments, a gene therapy vector is a viral vector. In some embodiments, an expression cassette having a promoter operably linked to a transgene encoding a minigene (e.g., mini-PCDH15) is flanked by one or more viral replication sequences, for example, lentiviral long terminal repeats (LTRs) or adeno-associated virus (AAV) inverted terminal 5 repeats (ITRs).

As used herein, "minigene" refers to an isolated nucleic acid sequence encoding a recombinant peptide or protein where one or more non-essential elements of the corresponding

gene encoding the naturally-occurring peptide or protein have been removed, and where the peptide or protein encoded by the minigene retains function of the corresponding naturally occurring peptide or protein. A "therapeutic minigene" refers to a minigene encoding a peptide or protein useful for treatment of a genetic disease, for example, protocadherin related 15 (PCDH15), dystrophin, dysferlin, Factor VIII, Amyloid precursor protein (APP), Tyrosinase (Tyr), etc. Minigenes are known in the art and are described, for example by Karpati and Acsadi (1994) Clin Invest Med 17(5):499-509; Plantier et al. (2001) Thromb Haemost. 86(2):596-603; and Xiao et al. (2007) World J. 15 Gastroenterol. 13(2):244-9.

I. Isolated Nucleic Acid

In some aspects, the disclosure provides isolated nucleic acids that are useful for expressing a mini-protocadherin related 15 (mini-PCDH15).

A "nucleic acid" sequence refers to a DNA or RNA sequence. In some embodiments, proteins and nucleic acids of the disclosure are isolated. As used herein, the term "isolated" means artificially produced. As used herein with respect to nucleic acids, the term "isolated" means: (i) amplified *in vitro* by, for example, polymerase chain reaction (PCR); (ii) recombinantly produced by cloning; (iii) purified, as by cleavage and gel separation; or (iv) synthesized by, for example, chemical synthesis. An isolated nucleic acid is one which is readily manipulable by recombinant DNA techniques well known in the art. Thus, a nucleotide sequence contained in a vector in which 5′ and 3′ restriction sites are known or for which polymerase chain reaction (PCR) primer sequences have been disclosed is considered isolated but a nucleic acid sequence existing in its native state in its natural host is not. An isolated nucleic acid may be substantially purified, but need not be. For example, a nucleic acid that is isolated within a cloning or expression vector is not pure in that it may comprise only a tiny percentage of the material in the cell in which it resides. Such a nucleic acid is isolated, however, as the term is used herein because it is readily manipulatable by standard techniques known to those of ordinary skill in the art.

The isolated nucleic acids of the invention may be recombinant adeno-associated virus (AAV) vectors (rAAV vectors). In some embodiments, an isolated nucleic acid as described by the disclosure comprises a region (*e.g.*, a first region) comprising a first adeno-associated virus (AAV) inverted terminal repeat (ITR). The isolated nucleic acid (*e.g.*, the recombinant

AAV vector) may be packaged into a capsid protein and administered to a subject and/or delivered to a selected target cell. "Recombinant AAV (rAAV) vectors" are typically composed of, at a minimum, a transgene and its regulatory sequences (*e.g.,* a promoter), and 5′ and 3′ AAV inverted terminal repeats (ITRs). The transgene may comprise, as disclosed elsewhere herein, a nucleic acid sequence encoding a protein (*e.g.*, mini-PCDH15).

Aspects of the present disclosure relates to an isolated nucleic acid comprising a transgene encoding a mini-PCDH15. The wild type PCDH15 coding sequence of ~5.8 kb is too large to fit into a single AAV capsid, which is limited to ~4.7 kb of transgene. Full length PCDH15 is encoded by wild type PCDH15 coding sequence. PCDH15 gene is a member of the cadherin superfamily. Family members encode integral membrane proteins that mediate calcium-dependent cell-cell adhesion. Full-length PCDH15 includes (From N-terminus to C-terminus): a signal peptide, eleven extracellular calcium-binding domains (EC domains, EC1-EC11), a membrane adjacent domain (MAD12), a transmembrane domain and a unique cytoplasmic domain. PCDH15 is expressed in several isoforms differing in their cytoplasmic domains, suggesting that alternative splicing regulates PCDH15 function in hair cells. There are three prominent splice isoforms of PCDH15 according to its unique cytoplasmic domain: CD1, CD2, and CD3. PCDH15 plays an essential role in maintenance of normal retinal and cochlear function. It is thought to interact with cadherin related 23 (CDH23) to form tip-link filaments.

An exemplary full length human PCDH15 extracellular portion (signal peptide + eleven EC domains) amino acid sequence is set forth in SEQ ID NO: 1 (EC1, EC3, EC5, EC7, EC9, and EC11 in boldface; signal peptide, EC2, EC4, EC6, EC8, and EC10 in regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT
KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV
MDANDN**TPTFPEISYDVYVYTDMRPGDSVIQLTAVDADEGSNGEITYEILVGAQGDFIINKTT**
GLITIAPGVEMIVGRTYALTVQAADNAPPAERRNSICTVYIEVLPPNNQSPPRFPQLMYSLEI
SEAMRVGAVLLNLQATDREGDSITYAIENGDPQRVFNLSETTGILTLGKALDRESTDRYILII
TASDGRPDGTSTATVNIVVTDVNDN**APVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQ**
VHYSLGNFNNLFRITSNGSIYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDD
NSPVFTNSTYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTGELSLL

RSLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDY**PPVFSKRIYKGMVAPDAV**
KGTPITTVYAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSGRVITRVNLNEEPTTIFK
LVVVAFDDGEPVMSSSATVKILVLHPGEIPRFTQEEYRPPPVSELATKGTMVGVISAAAINQS
IVYSIVSGNEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSLEVVLANLRVPSKSNTAK
VYIEIQDENNH**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGK**
EGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLD (SEQ ID NO: 1)

An exemplary nucleic acid sequence encoding full-length human PCDH15 extracellular portion:

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG
ATGGATGCAAATGATAACACGCCAACCTTCCCTGAAATATCCTATGATGTGTATGTTTATACA
GACATGAGACCTGGGGACAGTGTCATACAGCTCACTGCAGTCGACGCAGACGAAGGGTCAAAT
GGGGAGATCACATATGAAATCCTTGTTGGGGCTCAGGGAGACTTCATCATCAATAAAACAACA
GGGCTTATCACCATCGCTCCAGGGGTGGAAATGATAGTCGGGCGGACTTACGCACTCACGGTC
CAAGCAGCGGATAATGCTCCTCCTGCAGAGCGAAGGAACTCCATCTGCACTGTGTATATTGAA
GTGCTTCCACCAAATAATCAAAGCCCTCCTCGCTTCCCACAGCTGATGTATAGCCTTGAAATT
AGTGAAGCCATGAGGGTTGGTGCTGTTTTATTAAATCTACAGGCAACTGATCGAGAGGGAGAC
TCAATAACATATGCCATTGAGAATGGAGATCCTCAGAGAGTTTTTAATCTTTCAGAAACCACG
GGGATTCTAACCTTAGGGAAAGCACTGGACAGGGAAAGCACTGATCGCTACATTCTGATCATC
ACAGCTTCAGATGGCAGGCCAGATGGGACCTCAACTGCCACAGTAAACATAGTGGTGACAGAT
GTCAATGACAATGCTCCAGTGTTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTGGAAGAA

GAAGCCAATGCCTTTGTGGGTCAAGTAAAAGCAACAGACCCTGATGCTGGAATAAATGGTCAA
GTGCACTACAGTTTGGGTAACTTTAATAATCTTTTTCGTATCACATCCAATGGGAGCATTTAC
ACAGCAGTGAAGCTTAACAGAGAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCAACAGAT
GGAGCAGTACACCCTCGTCATTCAACTCTAACCTTGGCCATCAAGGTTTTGGACATTGATGAT
AACAGTCCTGTGTTCACCAATTCAACATACACTGTCCTTGTTGAAGAGAATTTGCCAGCTGGG
ACTACCATCCTTCAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTACCGGATA
AGAAGCCCAGAAGTGAAGCACTTTTTTGCACTACATCCATTTACAGGAGAACTATCGCTTTTA
AGGAGTTTAGATTATGAGGCATTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTAGAGGCC
TTTGATATTTATGGAACAATGCCACCTGGTATTGCTACTGTCACAGTGATTGTAAAGGATATG
AATGATTATCCTCCTGTCTTTAGTAAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTC
AAGGGTACACCTATCACAACAGTTTATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGT
CGTGTGAGGTATAGAGTAGATGATGTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAA
GAAGATTCTGGAAGAGTAATAACACGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAG
TTGGTGGTGGTTGCTTTTGATGATGGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATT
CTTGTCTTACATCCTGGTGAGATCCCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTA
AGTGAACTTGCCACCAAAGGGACCATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGT
ATTGTGTACTCCATTGTTTCAGGAAATGAAGAAGATACATTTGGAATTAATAACATCACAGGT
GTTATCTATGTGAATGGACCTCTGGATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAA
GCTGATTCCCTGGAAGTGGTCCTTGCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAA
GTATACATTGAGATTCAGGATGAAAATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATC
GGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAA
GATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAA
GAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATG
AGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGC
AAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGAT (SEQ ID NO: 2)

An exemplary amino acid sequence for full-length human PCDH15 (CD1 splice form cytoplasmic domain; EC1, EC3, EC5, EC7, EC9, EC11 and transmembrane-cytoplasmic domain in boldface; signal peptide, EC2, EC4, EC6, EC8, EC10 and MAD12 in regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT
KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV
MDANDN**TPTFPEISYDVYVYTDMRPGDSVIQLTAVDADEGSNGEITYEILVGAQGDFIINKTT**
GLITIAPGVEMIVGRTYALTVQAADNAPPAERRNSICTVYIEVLPPNNQSPPRFPQLMYSLEI
SEAMRVGAVLLNLQATDREGDSITYAIENGDPQRVFNLSETTGILTLGKALDRESTDRYILII
TASDGRPDGTSTATVNIVVTDVNDN**APVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQ**
VHYSLGNFNNLFRITSNGSIYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDD
NSPVFTNSTYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTGELSLL
RSLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDY**PPVFSKRIYKGMVAPDAV**
KGTPITTVYAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSGRVITRVNLNEEPTTIFK

LVVVAFDDGEPVMSSSATVKILVLHPGEIPRFTQEEYRPPPVSELATKGTMVGVISAAAINQS
IVYSIVSGNEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSLEVVLANLRVPSKSNTAK
VYIEIQDENNH**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGK**
EGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQVIVSNV
PPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAIDPQTN
RAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GALLALA**
FIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPPG
AHLYEELGDSSMHNLFLLYHFQQSRGNNSVSEDRKHQQVVMPFSSNTIEAHKSAHVDGSLKSN
KLKSARKFTFLSDEDDLSAHNPLYKENISQVSTNSDISQRTDFVDPFSPKIQAKSKSLRGPRE
KIQRLWSQSVSLPRRLMRKVPNRPEIIDLQQWQGTRQKAENENTGICTNKRGSSNPLLTTEEA
NLTEKEEIRQGETLMIEGTEQLKSLSSDSSFCFPRPHFSFSTLPTVSRTVELKSEPNVISSPA
ECSLELSPSRPCVLHSSLSRRETPICMLPIETERNIFENFAHPPNISPSACPLPPPPPISPPS
PPPAPAPLAPPPDISPFSLFCPPPSPPSIPLPLPPPTFFPLSVSTSGPPTPPLLPPFPTPLPP
PPPSIPCPPPPSASFLSTECVCITGVKCTTNLMPAEKIKSSMTQLSTTTVCKTDPQREPKGIL
RHVKNLAELEKSVANMYSQIEKNYLRTNVSELQTMCPSEVTNMEITSEQNKGSLNNIVEGTEK
QSHSQSTSL (SEQ ID NO: 53)

An exemplary nucleic acid sequence encoding full-length human PCDH15 (CD1 splice form, NM_001142763.2, includes coding and non-coding regions):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG
ATGGATGCAAATGATAACACGCCAACCTTCCCTGAAATATCCTATGATGTGTATGTTTATACA
GACATGAGACCTGGGGACAGTGTCATACAGCTCACTGCAGTCGACGCAGACGAAGGGTCAAAT
GGGGAGATCACATATGAAATCCTTGTTGGGGCTCAGGGAGACTTCATCATCAATAAAACAACA

GGGCTTATCACCATCGCTCCAGGGGTGGAAATGATAGTCGGGCGGACTTACGCACTCACGGTC
CAAGCAGCGGATAATGCTCCTCCTGCAGAGCGAAGGAACTCCATCTGCACTGTGTATATTGAA
GTGCTTCCACCAAATAATCAAAGCCCTCCTCGCTTCCCACAGCTGATGTATAGCCTTGAAATT
AGTGAAGCCATGAGGGTTGGTGCTGTTTTATTAAATCTACAGGCAACTGATCGAGAGGGAGAC
TCAATAACATATGCCATTGAGAATGGAGATCCTCAGAGAGTTTTTAATCTTTCAGAAACCACG
GGGATTCTAACCTTAGGGAAAGCACTGGACAGGGAAAGCACTGATCGCTACATTCTGATCATC
ACAGCTTCAGATGGCAGGCCAGATGGGACCTCAACTGCCACAGTAAACATAGTGGTGACAGAT
GTCAATGACAATGCTCCAGTGTTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTGGAAGAA
GAAGCCAATGCCTTTGTGGGTCAAGTAAAAGCAACAGACCCTGATGCTGGAATAAATGGTCAA
GTGCACTACAGTTTGGGTAACTTTAATAATCTTTTTCGTATCACATCCAATGGGAGCATTTAC
ACAGCAGTGAAGCTTAACAGAGAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCAACAGAT
GGAGCAGTACACCCTCGTCATTCAACTCTAACCTTGGCCATCAAGGTTTTGGACATTGATGAT
AACAGTCCTGTGTTCACCAATTCAACATACACTGTCCTTGTTGAAGAGAATTTGCCAGCTGGG
ACTACCATCCTTCAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTACCGGATA
AGAAGCCCAGAAGTGAAGCACTTTTTTGCACTACATCCATTTACAGGAGAACTATCGCTTTTA
AGGAGTTTAGATTATGAGGCATTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTAGAGGCC
TTTGATATTTATGGAACAATGCCACCTGGTATTGCTACTGTCACAGTGATTGTAAAGGATATG
AATGATTATCCTCCTGTCTTTAGTAAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTC
AAGGGTACACCTATCACAACAGTTTATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGT
CGTGTGAGGTATAGAGTAGATGATGTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAA
GAAGATTCTGGAAGAGTAATAACACGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAG
TTGGTGGTGGTTGCTTTTGATGATGGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATT
CTTGTCTTACATCCTGGTGAGATCCCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTA
AGTGAACTTGCCACCAAAGGGACCATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGT
ATTGTGTACTCCATTGTTTCAGGAAATGAAGAAGATACATTTGGAATTAATAACATCACAGGT
GTTATCTATGTGAATGGACCTCTGGATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAA
GCTGATTCCCTGGAAGTGGTCCTTGCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAA
GTATACATTGAGATTCAGGATGAAAATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATC
GGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAA
GATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAA
GAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATG
AGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGC
AAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTG
CCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAG
GAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCC
TTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAAC
AGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAA
GACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTG
ACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCC
TTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTT
AAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAA
CCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGT
GCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAATCTTTTCCTTCTCTACCATTTT
CAACAAAGCAGGGGAAATAACTCAGTCTCAGAAGACAGGAAACATCAACAAGTTGTGATGCCC
TTTTCTTCCAATACTATTGAGGCTCACAAGTCAGCTCATGTAGACGGATCACTTAAGAGCAAC
AAACTGAAGTCTGCAAGAAAATTCACATTTCTATCTGATGAGGATGACTTAAGTGCCCATAAT
CCCCTTTATAAGGAAAACATAAGTCAAGTATCAACAAATTCAGACATTTCACAGAGAACAGAT

TTTGTAGACCCATTTTCACCCAAAATACAAGCCAAGAGTAAGTCTCTGAGGGGCCCAAGAGAA
AAGATTCAGAGGCTGTGGAGTCAGTCAGTCAGCTTACCCAGGAGGCTGATGAGGAAAGTTCCA
AATAGACCAGAGATCATAGATCTGCAGCAGTGGCAAGGCACCAGGCAGAAAGCTGAAAATGAA
AACACTGGAATCTGTACAAACAAAAGAGGTAGCAGCAATCCATTGCTTACAACTGAAGAGGCA
AATTTGACAGAGAAAGAGGAAATAAGGCAAGGTGAAACACTGATGATAGAAGGAACAGAACAG
TTGAAATCTCTCTCTTCAGACTCTTCATTTTGCTTTCCCAGGCCTCACTTCTCATTCTCCACT
TTGCCAACTGTTTCAAGAACTGTGGAACTCAAATCAGAACCTAATGTCATCAGTTCTCCTGCT
GAGTGTTCCTTGGAACTTTCTCCTTCAAGGCCTTGTGTTTTACATTCTTCACTCTCTAGGAGA
GAGACACCTATTTGTATGTTACCTATTGAAACCGAAAGAAATATTTTTGAAAATTTTGCCCAT
CCACCAAACATCTCTCCTTCTGCCTGTCCCCTTCCCCCTCCTCCTCCTATTTCTCCTCCTTCT
CCTCCTCCTGCTCCTGCTCCTCTTGCTCCTCCTCCTGACATTTCTCCTTTTTCTCTTTTTTGT
CCTCCTCCCTCTCCTCCTTCTATCCCTCTTCCTCTTCCTCCTCCTACATTTTTTCCACTTTCC
GTTTCAACGTCTGGTCCCCCAACACCACCTCTTCTACCTCCATTTCCAACTCCTCTTCCTCCA
CCACCTCCTTCTATTCCTTGCCCTCCACCTCCTTCAGCTTCATTTCTGTCCACAGAGTGTGTC
TGTATAACAGGTGTTAAATGCACGACCAACTTGATGCCTGCCGAGAAAATTAAGTCCTCTATG
ACACAGCTATCAACAACGACAGTGTGTAAAACAGACCCTCAGAGAGAACCAAAAGGCATCCTC
AGACACGTTAAAAACTTAGCAGAACTTGAAAAATCAGTAGCTAACATGTACAGTCAAATAGAA
AAAAACTATCTACGCACAAATGTTTCAGAACTTCAAACTATGTGCCCTTCAGAAGTAACAAAT
ATGGAAATCACATCTGAACAAAACAAGGGGAGTTTGAACAATATTGTCGAGGGAACTGAAAAA
CAATCTCACAGTCAATCTACTTCACTGTAATGTTGCTTTTCTTATTTTAGTCGGGCAAACCTC
TTGTTGATCATAGTCTTCAAGTTGAACATCAAATTTGAACGTCAAAGAAGACTCTATTATTTT
ACCCCAAATTCAATGAAATGCAGTTTTTTTTCTCGTTTTTAATTTAAAAAGATATTAACCTCA
TCACTACTAACTCACTCATATAATAGATTTACCTTACTTTTTAAAAACTACAAAGTAGCATAA
TTTGTTCTACATTTATTTGAAAAGTAAGTAATTTTAATCTCTTTTTTAGTGGGAATATGTGGG
CATGAAAATTAGATACCCAACTTAAACCAAAGGCATGTCTATCATGTGGATGCAGTAACATTT
ACATTTAGTTTTTGATCGTAGTTTTATATGAATGTTCCAAGAAAAAAGCAGACTGTTACAAAT
AAGTTAAAACTGATATGATTGATAGGTTCTGTTTTTTCTTGAAGCCTATGTATTTGGTAAGAA
GAAATACTACCGAAGTAAAATATAATGTACCTAGATTGTAGGAGATGACAGACATAAGGTATT
TCAAAATAAATCTCAGGTGCTATAACATGTAGTCATCTGTTTTCTGATAAGAACATCTTTTAC
TCTGACTTGCTTTTATCTTAGTAGTATGCTTATGGATTTAGTAGTATGCTTATGGATTTGATA
AATCTTATACTTTTTCAGTTGCTGTCTTATTCTCTTTATTTCTCATTGTGCTTTCCCTTCCCT
TCTTTATAATGAAAATAAATCTTGAGTCGTTG (SEQ ID NO: 54)

An exemplary amino acid sequence for full-length human PCDH15 (CD2 splice form cytoplasmic domain; EC1, EC3, EC5, EC7, EC9, EC11 and transmembrane-cytoplasmic domain in boldface; signal peptide, EC2, EC4, EC6, EC8, EC10 and MAD12 in regular font). EC4 domain of the CD2 splice variant contains an additional 7 amino acid (italics) sequences compared to other splice forms:

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH

PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIED
*VPPSGVP*TKDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESE
PVIVNIQVMDANDN**TPTFPEISYDVYVYTDMRPGDSVIQLTAVDADEGSNGEITYEILVGAQG**
DFIINKTTGLITIAPGVEMIVGRTYALTVQAADNAPPAERRNSICTVYIEVLPPNNQSPPRFP
QLMYSLEISEAMRVGAVLLNLQATDREGDSITYAIENGDPQRVFNLSETTGILTLGKALDRES
TDRYILIITASDGRPDGTSTATVNIVVTDVNDN**APVFDPYLPRNLSVVEEEANAFVGQVKATD**
PDAGINGQVHYSLGNFNNLFRITSNGSIYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLA
IKVLDIDDNSPVFTNSTYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHP
FTGELSLLRSLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDY**PPVFSKRIYK**
GMVAPDAVKGTPITTVYAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSGRVITRVNLN
EEPTTIFKLVVVAFDDGEPVMSSSATVKILVLHPGEIPRFTQEEYRPPPVSELATKGTMVGVI
SAAAINQSIVYSIVSGNEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSLEVVLANLRV
PSKSNTAKVYIEIQDENNH**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLI**
IPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLD
MQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTV
YAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYT
E**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPP**
PPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEEEPKK
IKKPKVEIREPSEEEEVVVTIEKPPAAEPTYTTWKRARIFPMIFKKVRGLADKRGIVDLEGEE
WQRRLEEEDKDYLKLTLDQEEATESTVESEEESSSDYTEYSEEESEFSESETTEEESESETPS
EEEESSTPESEESESTESEGEKARKNIVLARRRPMVEEVKEVKGRKEEPQEEQKEPKMEEEEH
SEEEESGPAPVEESTDPEAQDIPEEGSAESASVEGGVESEEESESGSSSSSSESQSGGPWGYQ
VPAYDRSKNANQKKSPGANSEGYNTAL (SEQ ID NO: 55)

An exemplary nucleic acid sequence encoding full-length human PCDH15 (CD2 splice form, NM_001142769.3, includes coding and non-coding regions):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG

GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATGTT
CCACCCAGTGGAGTTCCTACAAAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCA
GTCTTCACCGTCACACAGACTGGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGG
GAAGAACAGCAAACTTACACCTTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCA
GTCATCGTCAATATTCAAGTGATGGATGCAAATGATAACACGCCAACCTTCCCTGAAATATCC
TATGATGTGTATGTTTATACAGACATGAGACCTGGGGACAGTGTCATACAGCTCACTGCAGTC
GACGCAGACGAAGGGTCAAATGGGGAGATCACATATGAAATCCTTGTTGGGGCTCAGGGAGAC
TTCATCATCAATAAAACAACAGGGCTTATCACCATCGCTCCAGGGGTGGAAATGATAGTCGGG
CGGACTTACGCACTCACGGTCCAAGCAGCGGATAATGCTCCTCCTGCAGAGCGAAGGAACTCC
ATCTGCACTGTGTATATTGAAGTGCTTCCACCAAATAATCAAAGCCCTCCTCGCTTCCCACAG
CTGATGTATAGCCTTGAAATTAGTGAAGCCATGAGGGTTGGTGCTGTTTTATTAAATCTACAG
GCAACTGATCGAGAGGGAGACTCAATAACATATGCCATTGAGAATGGAGATCCTCAGAGAGTT
TTTAATCTTTCAGAAACCACGGGGATTCTAACCTTAGGGAAAGCACTGGACAGGGAAAGCACT
GATCGCTACATTCTGATCATCACAGCTTCAGATGGCAGGCCAGATGGGACCTCAACTGCCACA
GTAAACATAGTGGTGACAGATGTCAATGACAATGCTCCAGTGTTTGATCCTTATCTGCCAAGA
AATTTATCTGTGGTGGAAGAAGAAGCCAATGCCTTTGTGGGTCAAGTAAAAGCAACAGACCCT
GATGCTGGAATAAATGGTCAAGTGCACTACAGTTTGGGTAACTTTAATAATCTTTTTCGTATC
ACATCCAATGGGAGCATTTACACAGCAGTGAAGCTTAACAGAGAAGTCAGGGACTACTATGAA
CTTGTTGTTGTGGCAACAGATGGAGCAGTACACCCTCGTCATTCAACTCTAACCTTGGCCATC
AAGGTTTTGGACATTGATGATAACAGTCCTGTGTTCACCAATTCAACATACACTGTCCTTGTT
GAAGAGAATTTGCCAGCTGGGACTACCATCCTTCAAATAGAGGCCAAAGATGTCGACCTTGGA
GCAAATGTGTCTTACCGGATAAGAAGCCCAGAAGTGAAGCACTTTTTTGCACTACATCCATTT
ACAGGAGAACTATCGCTTTTAAGGAGTTTAGATTATGAGGCATTTCCAGACCAAGAAGCAAGT
ATCACTTTTCTGGTAGAGGCCTTTGATATTTATGGAACAATGCCACCTGGTATTGCTACTGTC
ACAGTGATTGTAAAGGATATGAATGATTATCCTCCTGTCTTTAGTAAACGAATATACAAAGGG
ATGGTGGCTCCGGATGCAGTCAAGGGTACACCTATCACAACAGTTTATGCTGAAGATGCAGAC
CCTCCTGGATTACCTGCAAGTCGTGTGAGGTATAGAGTAGATGATGTACAGTTTCCTTACCCT
GCCAGTATTTTTGAAGTGGAAGAAGATTCTGGAAGAGTAATAACACGAGTCAATCTTAATGAA
GAACCTACAACAATTTTTAAGTTGGTGGTGGTTGCTTTTGATGATGGGGAGCCTGTGATGTCC
AGCAGTGCCACAGTGAAGATTCTTGTCTTACATCCTGGTGAGATCCCACGCTTCACACAGGAG
GAATATAGACCTCCTCCAGTAAGTGAACTTGCCACCAAAGGGACCATGGTTGGTGTAATTTCT
GCTGCTGCCATTAATCAAAGTATTGTGTACTCCATTGTTTCAGGAAATGAAGAAGATACATTT
GGAATTAATAACATCACAGGTGTTATCTATGTGAATGGACCTCTGGATTATGAGACCAGGACA
AGCTATGTACTTCGAGTCCAAGCTGATTCCCTGGAAGTGGTCCTTGCCAATCTCCGAGTTCCT
TCAAAAAGCAATACAGCTAAAGTATACATTGAGATTCAGGATGAAAATAATCATCCCCCAGTG
TTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTC
AGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATA
CCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACT
GCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGAC
TATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATG
CAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAG
ATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGA
GCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTAT
GCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGC
AAACTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAG
ATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAA
GGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTT

TTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAG
GCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCG
CCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAG
TATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATAT
GGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAGGAAGAGCCAAAGAAAATT
AAAAAACCAAAGGTTGAAATTAGAGAGCCTAGTGAGGAGGAAGAAGTAGTTGTAACTATCGAA
AAACCACCAGCAGCTGAGCCTACATACACAACATGGAAGAGAGCCAGAATATTCCCCATGATT
TTTAAGAAAGTTAGAGGATTAGCTGATAAAAGAGGAATCGTTGACCTTGAGGGTGAAGAGTGG
CAGAGACGCCTTGAGGAAGAAGATAAAGATTATTTGAAACTCACTCTGGACCAAGAGGAAGCA
ACAGAAAGCACTGTAGAATCAGAGGAGGAATCCTCCAGCGACTATACTGAATACAGTGAAGAA
GAGTCTGAGTTCAGTGAGTCTGAGACTACAGAAGAGGAATCTGAGTCAGAGACACCCTCTGAG
GAGGAGGAGAGTTCCACCCCTGAATCAGAAGAATCGGAATCCACAGAGTCAGAAGGAGAAAAA
GCAAGGAAAAACATTGTGCTTGCAAGAAGAAGGCCCATGGTTGAGGAGGTCAAGGAAGTCAAG
GGTAGGAAAGAGGAGCCACAAGAAGAACAAAAAGAACCTAAGATGGAAGAAGAAGAACACTCA
GAAGAAGAAGAAAGTGGACCAGCCCCTGTGGAAGAAAGTACAGACCCTGAAGCTCAAGATATC
CCTGAAGAGGGCAGTGCAGAATCAGCTTCGGTGGAAGGAGGTGTGGAAAGTGAGGAGGAATCA
GAATCAGGTAGTAGTAGCAGTAGTAGCGAAAGTCAGTCTGGAGGTCCATGGGGCTATCAGGTA
CCAGCGTATGACAGAAGCAAGAATGCAAACCAAAAGAAGTCGCCAGGAGCAAACTCTGAAGGT
TACAACACAGCACTTTGAAAGAGATCACAGTAGGTGGAAGTTTTGCTGTGATGAGTGCTCTCG
TGTGCAGTGCCTTCTGTGTGTTCTCCAAAGTGACACTTGAAAGGGAGGAAATTGATCAAGATT
TTGATATGACTTATGATCAGAAGCATGCCAGAAAAGTGAATATATATGTTGTCCAAATCCAT
(SEQ ID NO: 56)

An exemplary amino acid sequence for full-length human PCDH15 (CD3 splice form cytoplasmic domain; EC1, EC3, EC5, EC7, EC9, EC11 and transmembrane-cytoplasmic domain in boldface; signal peptide, EC2, EC4, EC6, EC8, EC10 and MAD12 in regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT
KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV
MDANDN**TPTFPEISYDVYVYTDMRPGDSVIQLTAVDADEGSNGEITYEILVGAQGDFIINKTT**
GLITIAPGVEMIVGRTYALTVQAADNAPPAERRNSICTVYIEVLPPNNQSPPRFPQLMYSLEI
SEAMRVGAVLLNLQATDREGDSITYAIENGDPQRVFNLSETTGILTLGKALDRESTDRYILII
TASDGRPDGTSTATVNIVVTDVNDN**APVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQ**
VHYSLGNFNNLFRITSNGSIYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDD
NSPVFTNSTYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTGELSLL
RSLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDY**PPVFSKRIYKGMVAPDAV**
KGTPITTVYAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSGRVITRVNLNEEPTTIFK
LVVVAFDDGEPVMSSSATVKILVLHPGEIPRFTQEEYRPPPVSELATKGTMVGVISAAAINQS
IVYSIVSGNEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSLEVVLANLRVPSKSNTAK
VYIEIQDENNH**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGK**

EGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQVIVSNV
PPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAIDPQTN
RAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GALLALA**
FIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPPG
AHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEWARKRMIKLVVDR
EYETSSTGEDSAPECQRNRLHHPSIHSNINGNIYIAQNGSVVRTRRACLTDNLKVASPVRLGG
PFKKLDKLAVTHEENVPLNTLSKGPFSTEKMNARPTLVTFAPCPVGTDNTAVKPLRNRLKSTV
EQESMIDSKNIKEALEFHSDHTQSDDEELWMGPWNNLHIPMTKL (SEQ ID NO: 57)

An exemplary nucleic acid sequence encoding full-length human PCDH15 (CD3 splice form, NM_001142771.2, includes coding and non-coding regions):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG
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GACATGAGACCTGGGGACAGTGTCATACAGCTCACTGCAGTCGACGCAGACGAAGGGTCAAAT
GGGGAGATCACATATGAAATCCTTGTTGGGGCTCAGGGAGACTTCATCATCAATAAAACAACA
GGGCTTATCACCATCGCTCCAGGGGTGGAAATGATAGTCGGGCGGACTTACGCACTCACGGTC
CAAGCAGCGGATAATGCTCCTCCTGCAGAGCGAAGGAACTCCATCTGCACTGTGTATATTGAA
GTGCTTCCACCAAATAATCAAAGCCCTCCTCGCTTCCCACAGCTGATGTATAGCCTTGAAATT
AGTGAAGCCATGAGGGTTGGTGCTGTTTTATTAAATCTACAGGCAACTGATCGAGAGGGAGAC
TCAATAACATATGCCATTGAGAATGGAGATCCTCAGAGAGTTTTTAATCTTTCAGAAACCACG
GGGATTCTAACCTTAGGGAAAGCACTGGACAGGGAAAGCACTGATCGCTACATTCTGATCATC
ACAGCTTCAGATGGCAGGCCAGATGGGACCTCAACTGCCACAGTAAACATAGTGGTGACAGAT
GTCAATGACAATGCTCCAGTGTTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTGGAAGAA

GAAGCCAATGCCTTTGTGGGTCAAGTAAAAGCAACAGACCCTGATGCTGGAATAAATGGTCAA
GTGCACTACAGTTTGGGTAACTTTAATAATCTTTTTCGTATCACATCCAATGGGAGCATTTAC
ACAGCAGTGAAGCTTAACAGAGAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCAACAGAT
GGAGCAGTACACCCTCGTCATTCAACTCTAACCTTGGCCATCAAGGTTTTGGACATTGATGAT
AACAGTCCTGTGTTCACCAATTCAACATACACTGTCCTTGTTGAAGAGAATTTGCCAGCTGGG
ACTACCATCCTTCAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTACCGGATA
AGAAGCCCAGAAGTGAAGCACTTTTTTGCACTACATCCATTTACAGGAGAACTATCGCTTTTA
AGGAGTTTAGATTATGAGGCATTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTAGAGGCC
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AAGGGTACACCTATCACAACAGTTTATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGT
CGTGTGAGGTATAGAGTAGATGATGTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAA
GAAGATTCTGGAAGAGTAATAACACGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAG
TTGGTGGTGGTTGCTTTTGATGATGGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATT
CTTGTCTTACATCCTGGTGAGATCCCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTA
AGTGAACTTGCCACCAAAGGGACCATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGT
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GTTATCTATGTGAATGGACCTCTGGATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAA
GCTGATTCCCTGGAAGTGGTCCTTGCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAA
GTATACATTGAGATTCAGGATGAAAATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATC
GGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAA
GATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAA
GAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATG
AGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGC
AAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTG
CCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAG
GAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCC
TTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAAC
AGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAA
GACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTG
ACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCC
TTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTT
AAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAA
CCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGT
GCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAGTATGAAATGCCTCAATATGGG
AGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATATGGTGAGGTGGTTGGTGAAGCT
GAGGAAGAATATGAGGAGGAAGAGTGGGCAAGAAAAAGAATGATCAAGTTAGTTGTTGATCGA
GAGTATGAAACCAGCTCAACTGGAGAAGACAGTGCTCCTGAATGTCAGAGAAACCGTCTTCAC
CATCCTAGTATCCACAGTAATATCAACGGCAATATATATATTGCACAGAATGGTTCTGTGGTG
AGAACCCGCCGTGCCTGCCTCACGGACAACTTAAAAGTTGCTTCCCCTGTTCGACTGGGAGGG
CCCTTTAAGAAACTAGACAAGTTGGCAGTGACACATGAGGAGAATGTACCTCTGAACACATTA
TCAAAGGGGCCATTTTCTACTGAAAAAATGAATGCAAGACCAACTCTGGTTACATTTGCCCCT
TGCCCTGTGGGGACTGACAATACAGCGGTGAAGCCACTAAGGAACAGGCTGAAAAGCACAGTT
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ACACAGTCTGATGATGAAGAGCTTTGGATGGGCCCCTGGAACAACCTCCATATACCAATGACA
AAACTGTGACCAATTTTTTAAAAGATATTTTAATTAATTTTTACTTACATTTTTAATAAACTG
TGCTTTTTATTGTCACTGAGAAAACAATGTATGGAATTTATATCATGCACACAAGCTAAAACT

TTGAACAATATGCTTTAAAATTTTAAGAGACAGATTTGCACTCACATTGTTATCAATTAATCG
TTTTTCCCAGAAAATCCTTTTGGACATACTTTCACTAAATAACCTATCGTTTAAACATTTAGC
TGTTTTGTTGGGTCTTGAATTTTTGTTCATTTTAATAAACAAGAAATAATTACTAAATAATCA
TTTATATTTTATTGATTAACATAGATTATGCTTTATTTCTAGCTCCACAAAACATTTTTAGTA
CATGTAATTTTATTTTCCATAGCCAAAAGGGCAAAAAAGAAGTAAGAGGATATTTACAGGCAA
TGAGTTTATACAGCTGCTGTCTATACTGCCCTAATTTTTAAAATGAAAGCTAGAATTGCAAAG
TAAAGTAAATGAGGGAATCACCTGTAAATAATTAATTATTTTAAATCATGAGCTTGTTTTCTT
TCTTTATTGTCCTGTATAAAGGTTTTCACATTTTACCATAAATACATTTATATCTTGACCCTT
TAGGAAACCACTTGAAGTCGTATGTCTTTTTATCAATATTATTTACAATATTCTCTTGTCCCT
TCATCTCATATCAAATATGGTAGATACTTTAGTTTAGTTTAATCACTTGAGGTTAAATAATTG
TTTGGAGCAACATGGAAATCTCACCCTTAGCAAAAGCTTTTAGGGAAGTGAGAAAGGTTCGAG
TAAGCAGTAATGCATCTAGAACGACAATTTCATAATGGAAGACATGGTGAGGTTAGGGAAGTC
TCACATTAATGTCACTAGACTTTAATAGTTTGTAAACCCAGCATATCAGAGTAAAGGAATTTG
GCAGGGTTGAAATGTATATAATATATAAAGCTTATAAAGGCTATGAATTCATAACTTCAAATG
TTGTGTTTAACTTCTTCCATTTTCAGGTTATTTATAGAATATTTTAATGCACATATTTATGTG
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GATTTTTTACCATTGAACAAAGCACAGTGTTTCATCATAAGTAGAAATGAAAACAGAATATCC
TTTAAAAAACTTGCCTTGTGTGTTGCTTATTTTCCAGATGATGTAAAAAGAATGAAACAATAT
AGATTAAGAGAATTCAGAATTCTATTGAATATTACTTAGTATGATATAGATGTAGCTCACTTC
AAATTTTGCACAGTATTGACCAAGTTCAGGTTTTAATGAAATTTCCTCATGCATGCTTAATAT
ATGGTTGAAGGACTGAATAATGCACTATTATTTATTCCCCTCTTACATGTTTCGCGTCTTAAA
AATTGTTTATTATTATGCTATTTCCTCATTTCCAAAGTGAATGAATTGTACTGACATAAACTT
GCCGACTTGTAAGAGTAGTATGTTTTTACTTCAGATTTCCAAGAAAATATTTGAGATCAAATA
CAGTAACATCTCATCTACCTTATTTTATTGAGAATTAATGCATTCCATACCCTTGCCAAAAAA
ACAAAACAAAACAAACAAACAAAAAAAAACCTAGTGGCATTAGCTAGATTAGAAACGTAGAAT
CATGACCACACCTCCTGGCCTGCCAAACAAGCATCCACATTTTCAAAAGATCCTAAGGTGGTT
TATATGCACATTAAATTTTGGAAGCAATGAAGTCCGGGGCTTATTCCTTCAGGCACCAAAGCA
ATGGTTTTTAGTATAGGATACTTTGTATAGGAATTAGATTAAGCATATATTTCCCTACTAATT
CAATCAGAGGTCATCGAATATAATTTAATATTATCTTGATACCCCCAGATCATCTCAGTCAGC
ATCCCTTGATATTCTCTCTATATACAGCTTCATGGCTGCGTTTTTGTCCTTTGATTTCTGGCT
GTGACATTTAACTTATTCTGTTGTTGTGCCTTTCTCACATTTTTTTCTTTCAGTTTATAGCTT
CTAGTATCCTGATGGGAAAGTTTGTGTTTTTTGTTTGTTTTCTTAATGTTGAAAAATCATGAA
GCTTAAGATGGGAATTAGGTACACGGATTCAACCAAATGTTTTGCGACTCTTAGACGCTTTCT
TTGGTTACCAGTAGATTTGGAAATATGATGTTGGCAGAAGTCTAGTGGCCTGACATATGAGAT
GTCACTGTATTTTAAACTACATTTTTTATGAGAAAATATGCAAAATTTTACAAGCCACTTAGC
AGACACATTTCAGTAATTTAAACTTGATCATTTCAGTAAAAACAATCATGAGGTCAATCATCT
GTTACTTAATGGAGATAGTATAAAGAGAAGCAGAATTTACACAGAGCAACCAAACCAAATATT
TGGTCAGTATATTTTTGGGTAACGTAGAGCAGCAAAATTATTACTAACTAAATAAATCTGGAT
CAATTAAATAGTTACTTTCATAGAACTTTCACTAGTCTATAAATCCCTGACTCAGGATTAAAA
CTGTGGAACCCAGAGGAAATACCCAGGTATGTTTAATCTTAAGAATACTTCATATAAATAACG
TTTCAATGTAAATATTTATAAAGAAATTGGTTGTTATTTTTCCTAGGAAGGTGTAGGAAGGTT
TTCTTGTTGTTCTCAATCAGCACTAGCTTCAATCAGGCAGAAGAAACAGCAGGTCTTGGCTAA
TCGAGGTGAGAACAGAATGATGTAATGACTAATATTGCAACCCGTTGATTTTAGAAGGTCTTG
TGGGCATTAAGGGAAAGCAGAGGAAGAATGAGAAAATATGGTCAGAGTGACATAGGACATTTG
TGACTTAATGACCATCGAATCACAGGTGTTAATCTCCCTCTCTCAATTTGTCTTTCTCATTAA
TTACAGACTCTGAGAGTTGTCATAGAATTGCAACCGTAGGTTGGCCAAAACCATCTTTTTAAA
ATACAGAAGAAAGTTTGCCTTGAATTTTATATGTGATATGTCATTCATGTTATTTTACCACAT

TGTTCACAGGGATGTTAAAGACTATTATTTACTTAAGTGGTTGTTCCAAAGGTGATTCAGTAG
TTACCATTAAAATATTATTTAAAAACATTTTTATATCATAGAGCCAGAAGTAATTGAATATTG
ACTCTCGAGGGAAGACATTTTCTGTCTTTTATTTCATGAGCTTTGATTTTTCTCTTTCTCTGC
TTCACCTTCTGCACTTTATACCTTAAGTGGGATTTATATACCACTTGAATTTAATTAGCAAAA
TAGGCAAAAAGTGCTAATAATCTATTCTCAGGGCAGATGCCTATTGGTGCCTGCAAATTACAC
AGCGATAAGGCTGAAGGATAGGTTCAAAATAATGTTGAGGACTTACACATTTTATAGATAGTT
TCTTTCTATTCCCAAATGGTATGTGAAATTTTTGTTCTATTTTTTTTATTGGTTTTCAATAGT
TAATTTTGATCTTTATCATAAGAAGCTTTAGTTATAGACTGGTATTTTTTTCATTGCAATCTA
CTTTAAATTTATGGTCAGTTAAGCACATGTATGGAAGATTCGAACATTGTCTATAGTTTGAAA
AATCTATCAACACCTTCACTGCTTTCCCAATTTCTTTATCCAAATACCTGTTCTTCCTTAACA
AATATTATGTTACTGTATAAGAATCTGAATTAGAAGTTTTAAGTTAAAATGCATTGTTATTCA
CTACACAATGTTTCAAAAATAAATTTTCATTTGAAAA (SEQ ID NO: 58)

The present disclosure, at least in part, is related to designing a mini-PCDH15 coding sequence that is small enough to fit into an AAV genome. PCDH15 binds to CDH23 at its N-terminal and to TMC1 and LHFPL5 near its C terminal. The intervening EC domains may not be essential for its function. A mini-PCDH15, as used herein, refers to a PCDH15 protein with one or more deletions of non-essential domains (*e.g.,* intervening EC domains) that retains normal PCDH15 function (*e.g.*, binding to CDH12). Exemplary human PCDH15 signal peptides, each of EC domains (EC1-EC11), MAD12 and transmembrane-cytoplasmic domain amino acid sequences and nucleic acid sequences encoding each of the domains are set forth in SEQ ID NOs: 3-30 and SEQ ID NO: 59-62, 119 and 120.

Signaling peptide sequence
MFRQFYLWTCLASGIILGSLFEICLG (SEQ ID NO: 3)

EC1 amino acid sequence
QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVDNMLIKGTAGGPDPTIELSLKDNVDYW
VLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCINKKVGTIIYHEVRIVVRDRNDN
(SEQ ID NO: 4)

EC2 amino acid sequence
SPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPNGQIEYVIQYNPDDPTSNDTFEI
PLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTTTTTLTVDVLDGDDL (SEQ ID
NO: 5)

EC3 amino acid sequence
GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQDRNIQPPSDRPGILY
SILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGHPLPAFAGLHIEILD
ENNQ (SEQ ID NO: 6)

EC4 amino acid sequence
SPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDTKDPELHLFLNDYTSVFTV
TQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQVMDANDN (SEQ ID NO: 7)

EC4 CD2 splicing variant amino acid sequence
SPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIED*VPPSGVP*TKDPELHLFLND
YTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQVMDANDN (SEQ ID NO: 119)

EC5 amino acid sequence
TPTFPEISYDVYVYTDMRPGDSVIQLTAVDADEGSNGEITYEILVGAQGDFIINKTTGLITIA
PGVEMIVGRTYALTVQAADNAPPAERRNSICTVYIEVLPPNNQ (SEQ ID NO: 8)

EC6 amino acid sequence
SPPRFPQLMYSLEISEAMRVGAVLLNLQATDREGDSITYAIENGDPQRVFNLSETTGILTLGK
ALDRESTDRYILIITASDGRPDGTSTATVNIVVTDVNDN (SEQ ID NO: 9)

EC7 amino acid sequence
APVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQVHYSLGNFNNLFRITSNGSIYTAVK
LNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDDN (SEQ ID NO: 10)

EC8 amino acid sequence
SPVFTNSTYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTGELSLLR
SLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDY (SEQ ID NO: 11)

EC9 amino acid sequence
PPVFSKRIYKGMVAPDAVKGTPITTVYAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDS
GRVITRVNLNEEPTTIFKLVVVAFDDGEPVMSSSATVKILVLHPGE (SEQ ID NO: 12)

EC10 amino acid sequence
IPRFTQEEYRPPPVSELATKGTMVGVISAAAINQSIVYSIVSGNEEDTFGINNITGVIYVNGP
LDYETRTSYVLRVQADSLEVVLANLRVPSKSNTAKVYIEIQDENNH (SEQ ID NO: 13)

EC11 amino acid sequence
PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETYTGL
IKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLD (SEQ ID NO: 14)

MAD12 amino acid sequence
MQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTV
YAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYT
E (SEQ ID NO: 15)

Transmembrane-cytoplasmic domain amino acid sequence (CD1 isoform)
GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPP
PPPPPPGAHLYEELGDSSMHNLFLLYHFQQSRGNNSVSEDRKHQQVVMPFSSNTIEAHKSAHV
DGSLKSNKLKSARKFTFLSDEDDLSAHNPLYKENISQVSTNSDISQRTDFVDPFSPKIQAKSK

SLRGPREKIQRLWSQSVSLPRRLMRKVPNRPEIIDLQQWQGTRQKAENENTGICTNKRGSSNP
LLTTEEANLTEKEEIRQGETLMIEGTEQLKSLSSDSSFCFPRPHFSFSTLPTVSRTVELKSEP
NVISSPAECSLELSPSRPCVLHSSLSRRETPICMLPIETERNIFENFAHPPNISPSACPLPPP
PPISPPSPPPAPAPLAPPPDISPFSLFCPPPSPPSIPLPLPPPTFFPLSVSTSGPPTPPLLPP
FPTPLPPPPPSIPCPPPPSASFLSTECVCITGVKCTTNLMPAEKIKSSMTQLSTTTVCKTDPQ
REPKGILRHVKNLAELEKSVANMYSQIEKNYLRTNVSELQTMCPSEVTNMEITSEQNKGSLNN
IVEGTEKQSHSQSTSL (SEQ ID NO: 16)

Transmembrane-cytoplasmic domain amino acid sequence (CD2 isoform)
GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPP
PPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEEEPKKI
KKPKVEIREPSEEEEVVVTIEKPPAAEPTYTTWKRARIFPMIFKKVRGLADKRGIVDLEGEEW
QRRLEEEDKDYLKLTLDQEEATESTVESEEESSSDYTEYSEEESEFSESETTEEESESETPSE
EEESSTPESEESESTESEGEKARKNIVLARRRPMVEEVKEVKGRKEEPQEEQKEPKMEEEEHS
EEEESGPAPVEESTDPEAQDIPEEGSAESASVEGGVESEEESESGSSSSSSESQSGGPWGYQV
PAYDRSKNANQKKSPGANSEGYNTAL (SEQ ID NO: 59)

Transmembrane-cytoplasmic domain amino acid sequence (CD3 isoform)
GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPP
PPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEWARKRM
IKLVVDREYETSSTGEDSAPECQRNRLHHPSIHSNINGNIYIAQNGSVVRTRRACLTDNLKVA
SPVRLGGPFKKLDKLAVTHEENVPLNTLSKGPFSTEKMNARPTLVTFAPCPVGTDNTAVKPLR
NRLKSTVEQESMIDSKNIKEALEFHSDHTQSDDEELWMGPWNNLHIPMTKL (SEQ ID NO:
60)

Signaling peptide coding sequence
ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGC (SEQ ID NO: 17)

EC1 coding sequence
CAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGAGGACCACCAGCTACC
ATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGACAACATGCTGATCAAA
GGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGATAATGTGGATTACTGG
GTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGAAGAGTTCTGGATAGA
GATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATCAACAAAAAAGTGGGC
ACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGACAAC (SEQ ID NO:
18)

EC2 coding sequence
TCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGTACC
ACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAATGGA
CAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAAATT
CCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACTCGC
TACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACCACC
ACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTG (SEQ ID NO: 19)

EC3 coding sequence

GGTCCAATGTTTCTTCCTTGTGTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTAT
CAAGCTGCCATACCTGAGTTGAGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCA
ATCCAAGCCATTGATCAGGACCGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTAT
TCCATCCTTGTTGGGACTCCTGAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCA
GAACTTAGTCTCCTGGAGCCAGTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAG
GCTGAACAAGACAATGGTCATCCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGAT
GAAAACAATCAA (SEQ ID NO: 20)

EC4 coding sequence
AGTCCATATTTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCA
ACCATTTCGGACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATA
GAAGATACAAAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTC
ACACAGACTGGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAA
ACTTACACCTTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAAT
ATTCAAGTGATGGATGCAAATGATAAC (SEQ ID NO: 21)

EC4 CD2 splice form coding sequence:
AGTCCATATTTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCA
ACCATTTCGGACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATA
GAAGATGTTCCACCCAGTGGAGTTCCTACAAAAGACCCAGAGCTTCACCTTTTTCTGAATGAC
TACACCTCAGTCTTCACCGTCACACAGACTGGTATTACTCGCTACCTCACCTTACTTCAACCA
GTGGACAGGGAAGAACAGCAAACTTACACCTTTTCGATAACAGCATTTGATGGTGTACAAGAA
AGTGAGCCAGTCATCGTCAATATTCAAGTGATGGATGCAAATGATAAC (SEQ ID NO: 120)

EC5 coding sequence
ACGCCAACCTTCCCTGAAATATCCTATGATGTGTATGTTTATACAGACATGAGACCTGGGGAC
AGTGTCATACAGCTCACTGCAGTCGACGCAGACGAAGGGTCAAATGGGGAGATCACATATGAA
ATCCTTGTTGGGGCTCAGGGAGACTTCATCATCAATAAAACAACAGGGCTTATCACCATCGCT
CCAGGGGTGGAAATGATAGTCGGGCGGACTTACGCACTCACGGTCCAAGCAGCGGATAATGCT
CCTCCTGCAGAGCGAAGGAACTCCATCTGCACTGTGTATATTGAAGTGCTTCCACCAAATAAT
CAA (SEQ ID NO: 22)

EC6 coding sequence
AGCCCTCCTCGCTTCCCACAGCTGATGTATAGCCTTGAAATTAGTGAAGCCATGAGGGTTGGT
GCTGTTTTATTAAATCTACAGGCAACTGATCGAGAGGGAGACTCAATAACATATGCCATTGAG
AATGGAGATCCTCAGAGAGTTTTTAATCTTTCAGAAACCACGGGGATTCTAACCTTAGGGAAA
GCACTGGACAGGGAAAGCACTGATCGCTACATTCTGATCATCACAGCTTCAGATGGCAGGCCA
GATGGGACCTCAACTGCCACAGTAAACATAGTGGTGACAGATGTCAATGACAAT (SEQ ID NO: 23)

EC7 coding sequence
GCTCCAGTGTTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTGGAAGAAGAAGCCAATGCC
TTTGTGGGTCAAGTAAAAGCAACAGACCCTGATGCTGGAATAAATGGTCAAGTGCACTACAGT
TTGGGTAACTTTAATAATCTTTTTCGTATCACATCCAATGGGAGCATTTACACAGCAGTGAAG
CTTAACAGAGAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCAACAGATGGAGCAGTACAC
CCTCGTCATTCAACTCTAACCTTGGCCATCAAGGTTTTGGACATTGATGATAAC (SEQ ID NO: 24)

EC8 coding sequence
AGTCCTGTGTTCACCAATTCAACATACACTGTCCTTGTTGAAGAGAATTTGCCAGCTGGGACT
ACCATCCTTCAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTACCGGATAAGA
AGCCCAGAAGTGAAGCACTTTTTTGCACTACATCCATTTACAGGAGAACTATCGCTTTTAAGG
AGTTTAGATTATGAGGCATTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTAGAGGCCTTT
GATATTTATGGAACAATGCCACCTGGTATTGCTACTGTCACAGTGATTGTAAAGGATATGAAT
GATTAT (SEQ ID NO: 25)

EC9 coding sequence
CCTCCTGTCTTTAGTAAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTCAAGGGTACA
CCTATCACAACAGTTTATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGTCGTGTGAGG
TATAGAGTAGATGATGTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAAGAAGATTCT
GGAAGAGTAATAACACGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAGTTGGTGGTG
GTTGCTTTTGATGATGGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATTCTTGTCTTA
CATCCTGGTGAG (SEQ ID NO: 26)

EC10 coding sequence
ATCCCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTAAGTGAACTTGCCACCAAAGGG
ACCATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGTATTGTGTACTCCATTGTTTCA
GGAAATGAAGAAGATACATTTGGAATTAATAACATCACAGGTGTTATCTATGTGAATGGACCT
CTGGATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAAGCTGATTCCCTGGAAGTGGTC
CTTGCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAAGTATACATTGAGATTCAGGAT
GAAAATAATCAT (SEQ ID NO: 27)

EC11 coding sequence
CCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACT
TCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGA
CTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTT
ATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCA
ACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAG
CTGGAT (SEQ ID NO: 28)

MAD12 coding sequence
ATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACA
GAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATT
GGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTC
TATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGAT
GGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTG
GAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACA
GAA (SEQ ID NO: 29)

Transmembrane-cytoplasmic domain coding sequence (CD1 isoform)
GGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTT
TTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAG
GCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCG
CCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAT

CTTTTCCTTCTCTACCATTTTCAACAAAGCAGGGGAAATAACTCAGTCTCAGAAGACAGGAAA
CATCAACAAGTTGTGATGCCCTTTTCTTCCAATACTATTGAGGCTCACAAGTCAGCTCATGTA
GACGGATCACTTAAGAGCAACAAACTGAAGTCTGCAAGAAAATTCACATTTCTATCTGATGAG
GATGACTTAAGTGCCCATAATCCCCTTTATAAGGAAAACATAAGTCAAGTATCAACAAATTCA
GACATTTCACAGAGAACAGATTTTGTAGACCCATTTTCACCCAAAATACAAGCCAAGAGTAAG
TCTCTGAGGGGCCCAAGAGAAAAGATTCAGAGGCTGTGGAGTCAGTCAGTCAGCTTACCCAGG
AGGCTGATGAGGAAAGTTCCAAATAGACCAGAGATCATAGATCTGCAGCAGTGGCAAGGCACC
AGGCAGAAAGCTGAAAATGAAAACACTGGAATCTGTACAAACAAAAGAGGTAGCAGCAATCCA
TTGCTTACAACTGAAGAGGCAAATTTGACAGAGAAAGAGGAAATAAGGCAAGGTGAAACACTG
ATGATAGAAGGAACAGAACAGTTGAAATCTCTCTCTTCAGACTCTTCATTTTGCTTTCCCAGG
CCTCACTTCTCATTCTCCACTTTGCCAACTGTTTCAAGAACTGTGGAACTCAAATCAGAACCT
AATGTCATCAGTTCTCCTGCTGAGTGTTCCTTGGAACTTTCTCCTTCAAGGCCTTGTGTTTTA
CATTCTTCACTCTCTAGGAGAGAGACACCTATTTGTATGTTACCTATTGAAACCGAAAGAAAT
ATTTTTGAAAATTTTGCCCATCCACCAAACATCTCTCCTTCTGCCTGTCCCCTTCCCCCTCCT
CCTCCTATTTCTCCTCCTTCTCCTCCTCCTGCTCCTGCTCCTCTTGCTCCTCCTCCTGACATT
TCTCCTTTTTCTCTTTTTTGTCCTCCTCCCTCTCCTCCTTCTATCCCTCTTCCTCTTCCTCCT
CCTACATTTTTTCCACTTTCCGTTTCAACGTCTGGTCCCCCAACACCACCTCTTCTACCTCCA
TTTCCAACTCCTCTTCCTCCACCACCTCCTTCTATTCCTTGCCCTCCACCTCCTTCAGCTTCA
TTTCTGTCCACAGAGTGTGTCTGTATAACAGGTGTTAAATGCACGACCAACTTGATGCCTGCC
GAGAAAATTAAGTCCTCTATGACACAGCTATCAACAACGACAGTGTGTAAAACAGACCCTCAG
AGAGAACCAAAAGGCATCCTCAGACACGTTAAAAACTTAGCAGAACTTGAAAAATCAGTAGCT
AACATGTACAGTCAAATAGAAAAAAACTATCTACGCACAAATGTTTCAGAACTTCAAACTATG
TGCCCTTCAGAAGTAACAAATATGGAAATCACATCTGAACAAAACAAGGGGAGTTTGAACAAT
ATTGTCGAGGGAACTGAAAAACAATCTCACAGTCAATCTACTTCACTGTAA (SEQ ID NO: 30)

Transmembrane-cytoplasmic domain coding sequence (CD2 isoform)

GGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTT
TTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAG
GCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCG
CCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAG
TATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATAT
GGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAGGAAGAGCCAAAGAAAATT
AAAAAACCAAAGGTTGAAATTAGAGAGCCTAGTGAGGAGGAAGAAGTAGTTGTAACTATCGAA
AAACCACCAGCAGCTGAGCCTACATACACAACATGGAAGAGAGCCAGAATATTCCCCATGATT
TTTAAGAAAGTTAGAGGATTAGCTGATAAAAGAGGAATCGTTGACCTTGAGGGTGAAGAGTGG
CAGAGACGCCTTGAGGAAGAAGATAAAGATTATTTGAAACTCACTCTGGACCAAGAGGAAGCA
ACAGAAAGCACTGTAGAATCAGAGGAGGAATCCTCCAGCGACTATACTGAATACAGTGAAGAA
GAGTCTGAGTTCAGTGAGTCTGAGACTACAGAAGAGGAATCTGAGTCAGAGACACCCTCTGAG
GAGGAGGAGAGTTCCACCCCTGAATCAGAAGAATCGGAATCCACAGAGTCAGAAGGAGAAAAA
GCAAGGAAAAACATTGTGCTTGCAAGAAGAAGGCCCATGGTTGAGGAGGTCAAGGAAGTCAAG
GGTAGGAAAGAGGAGCCACAAGAAGAACAAAAAGAACCTAAGATGGAAGAAGAAGAACACTCA
GAAGAAGAAGAAAGTGGACCAGCCCCTGTGGAAGAAAGTACAGACCCTGAAGCTCAAGATATC
CCTGAAGAGGGCAGTGCAGAATCAGCTTCGGTGGAAGGAGGTGTGGAAAGTGAGGAGGAATCA
GAATCAGGTAGTAGTAGCAGTAGTAGCGAAAGTCAGTCTGGAGGTCCATGGGGCTATCAGGTA
CCAGCGTATGACAGAAGCAAGAATGCAAACCAAAAGAAGTCGCCAGGAGCAAACTCTGAAGGT
TACAACACAGCACTTTGA (SEQ ID NO: 61)

Transmembrane-cytoplasmic domain coding sequence (CD3 isoform)

GGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTT
TTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAG
GCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCG
CCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAG
TATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATAT
GGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAGTGGGCAAGAAAAAGAATG
ATCAAGTTAGTTGTTGATCGAGAGTATGAAACCAGCTCAACTGGAGAAGACAGTGCTCCTGAA
TGTCAGAGAAACCGTCTTCACCATCCTAGTATCCACAGTAATATCAACGGCAATATATATATT
GCACAGAATGGTTCTGTGGTGAGAACCCGCCGTGCCTGCCTCACGGACAACTTAAAAGTTGCT
TCCCCTGTTCGACTGGGAGGGCCCTTTAAGAAACTAGACAAGTTGGCAGTGACACATGAGGAG
AATGTACCTCTGAACACATTATCAAAGGGGCCATTTTCTACTGAAAAAATGAATGCAAGACCA
ACTCTGGTTACATTTGCCCCTTGCCCTGTGGGGACTGACAATACAGCGGTGAAGCCACTAAGG
AACAGGCTGAAAAGCACAGTTGAACAGGAGTCCATGATTGACAGTAAGAACATCAAGGAGGCT
TTGGAATTTCATAGTGACCACACACAGTCTGATGATGAAGAGCTTTGGATGGGCCCCTGGAAC
AACCTCCATATACCAATGACAAAACTGTGA (SEQ ID NO: 62)

In some embodiments, the coding sequence for mini-PCDH15 is less than 5000, 4500, 4000, 3500, 3000, 2500, 2000, or less nucleic acids. In some embodiments, the coding sequence for mini-PCDH15 is less than 5000 nucleic acids. In some embodiments, the coding sequence for mini-PCDH15 is less than 4600 base pairs. In other embodiments, the coding sequence for mini-PCDH15 is less than 3000 base pairs. The mini-PCDH15, as described herein, is small enough to be packaged into a single AAV-genome, and maintain the biological function of PCDH15.

In some embodiments, the mini-PCDH15 comprises a truncated extracellular portion of the full-length PCDH15. A truncated extracellular portion, as used herein, refers to an extracellular portion of a protein, which is shorter by at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 100, 200, 300, 400, 500, 600, 700, 800, or more amino acids less than the extracellular portion of a full-length protein. In some instances, the mini-PCDH15 comprises an extracellular portion at least 100, 200, 300, 400, 500. 600, 700, 800, 900 or 1000 amino acids less than full length PCDH15.

In some embodiments, the extracellular portion of a full-length PCDH15 comprises 11 extracellular calcium-binding (EC) domains. In some embodiments, the mini-PCDH15 does not comprise one or more EC domains compared to a full-length PCDH15. The full length PCDH15 includes 11 EC domains. In some embodiments, the mini-PCDH15 can have at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 less EC domains compared to full-length PCDH15. In some embodiments, the mini-PCDH15 can have 3 EC domains less than full-length PCDH15. In

some embodiments, the mini-PCDH15 can have 4 EC domains less than full-length PCDH15. In some embodiments, the mini-PCDH15 can have 5 EC domains less than full-length PCDH15. In some embodiments, the mini-PCDH15 can have 6 EC domains less than full-length PCDH15. In some embodiments, the mini-PCDH15 can have 7 EC domains less than full-length PCDH15. In some embodiments, the mini-PCDH15 can have 8 EC domains less than full-length PCDH15. In some embodiments, the mini-PCDH15 can have 9 EC domains less than full-length PCDH15. In some embodiments, the mini-PCDH15 can have 10 EC domains less than full-length PCDH15.

Exemplary EC domain sequences are set forth in SEQ ID NOs: 4 to 14. An exemplary full-length PCDH15 extracellular domain comprises 11 EC domains (*e.g.*, EC1 at amino acid residues 27-148 of SEQ ID NO: 1; EC2 at amino acid residues 149-266 of SEQ ID NO: 1; EC3 at amino acid residues 267-396 of SEQ ID NO: 1; EC4 at amino acid residues 397-510 of SEQ ID NO: 1; EC5 at amino acid residues 511-616 of SEQ ID NO: 1; EC6 at amino acid residues 617-718 of SEQ ID NO: 1; EC7 at amino acid residues 719-820 of SEQ ID NO: 1; EC8 at amino acid residues 821-927 of SEQ ID NO: 1; EC9 at amino acid residues 928-1036 of SEQ ID NO: 1; EC10 at amino acid residues 1037-1145 of SEQ ID NO: 1; and EC11 at amino acid residues 1146-1252 of SEQ ID NO: 1).

Any of the mini-PCDH15, as described herein, may further comprises a MAD12 domain, a transmembrane domain and a cytoplasmic domain. In some embodiments, the cytoplasmic domain of PCDH15 is a splice isoform. In some embodiments, the splice isoform of PCDH15 is CD1, CD2 or CD3 isoforms. In some embodiments, the transmembrane-cytoplasmic domain of the splice isoform comprises an amino acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 16. In some embodiments, the transmembrane-cytoplasmic domain of the splice isoform comprises an amino acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 59. In some embodiments, the transmembrane-cytoplasmic domain of the splice isoform comprises an amino acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 60. In some embodiments, the CD2 splice form comprises an EC4 domain as set forth in amino acid sequence of SEQ ID NO:

119. Any of the mini-PCDH15 described herein, when having EC4 domain, may include the EC4 domain of SEQ ID NO: 7 or SEQ ID NO: 119.

An exemplary full-length human PCDH15 comprises 11 EC domains, MAD12 domain and TM-cytoplasmic domain (*e.g.*, full length human PCDH15 CD1 splice form set forth in SEQ ID NO: 53, full length human PCDH15 CD2 splice form set forth in SEQ ID NO: 55, and full length human PCDH15 CD3 splice form set forth in SEQ ID NO: 57). In some embodiments, EC1 comprises amino acid residues 27-148 of SEQ ID NOs: 53, 55, and 57; EC2 comprises amino acid residues 149-266 of SEQ ID NOs: 53, 55, and 57; EC3 comprises amino acid residues 267-396 of SEQ ID NOs: 53, 55, and 57; EC4 comprises amino acid residues 397-510 of SEQ ID NOs: 53, and 57 or amino acid residues 397-517 of SEQ ID NO: 55; EC5 comprises amino acid residues 511-616 of SEQ ID NOs: 53, and 57 or amino acid residues 518-623 of SEQ ID NO: 55; EC6 comprises amino acid residues 617-718 of SEQ ID NOs: 53, and 57 or amino acid residues 624-725 of SEQ ID NO: 55; EC7 comprises amino acid residues 719-820 of SEQ ID NOs: 53, and 57 or amino acid residues 726-827 of SEQ ID NO: 55; EC8 comprises amino acid residues 821-927 of SEQ ID NOs: 53, and 57 or amino acid residues 828-934 of SEQ ID NO: 55; EC9 comprises amino acid residues 928-1036 of SEQ ID NOs: 53, and 57 or amino acid residues 935-1043 of SEQ ID NO: 55; EC10 comprises amino acid residues 1037-1145 of SEQ ID NOs: 53, and 57 or amino acid residues 1044-1152 of SEQ ID NO: 55; and EC11 comprises amino acid residues 1146-1252 of SEQ ID NOs: 53 and 57 or amino acid residues 1153-1259 of SEQ ID NO: 55.

In some embodiments, the mini-PCDH15 does not comprise amino acid residues 719 to 820 of SEQ ID NO: 1, 53, or 57, or amino acid residues 726-827 of SEQ ID NO: 55 (EC7). Alternatively or in addition, the mini-PCDH15 may not comprise amino acid residues 397 to 510 of SEQ ID NOs: 1, 53 or 57, or amino acid residues 397-517 of SEQ ID NO: 55 (EC4). Alternatively or in addition, the mini-PCDH15 may not comprise amino acid residues 821 to 927 of SEQ ID NOs: 1, 53 or 57, or amino acid residues 828-934 of SEQ ID NO: 55 (EC8). Alternatively or in addition, the mini-PCDH15 may not comprise amino acid residues 511 to 616 of SEQ ID NOs: 1, 53 or 57, or amino acid residues 518-623 of SEQ ID NO: 55 (EC5). Alternatively or in addition, the mini-PCDH15 may not comprise amino acid residues 617 to 718 of SEQ ID NOs: 1, 53 or 57, or amino acid residues 624-725 of SEQ ID NO: 55 (EC6). Alternatively or in addition, the mini-PCDH15 may not comprise amino acid residues 928 to

1036 of SEQ ID NOs: 1, 53 or 57, or amino acid residues 935-1043 of SEQ ID NO: 55 (EC9). Alternatively or in addition, the mini-PCDH15 may not comprise amino acid residues 1037 to 1145 of SEQ ID NOs: 1, 53, 55 or 57 (EC10). Alternatively or in addition, the mini-PCDH15 may not comprise amino acid residues 27 to 148 of SEQ ID NOs: 1, 53, 55 or 57 (EC1). Alternatively or in addition, the mini-PCDH15 may not comprise amino acid residues 149-266 of SEQ ID NOs: 1, 53, 55 or 57 (EC2). Alternatively or in addition, the mini-PCDH15 may not comprise amino acid residues 267 to 396 of SEQ ID NOs: 1, 53, 55 or 57 (EC3). Alternatively or in addition, the mini-PCDH15 may not comprise amino acid residues 1146 to 1252 of SEQ ID NOs: 1, 53, or 57, or amino acid residues 1153-1259 of SEQ ID NO: 55(EC11).

In some embodiments, the mini-PCDH15 comprises one EC domain in the extracellular region (*e.g.*, EC1, EC2, EC3, EC4, EC5, EC6, EC7, EC8, EC9, EC10 or EC11) of a full length PCDH15 extracellular domain set forth in SEQ ID NO: 1 or full length PCDH15 set forth in SEQ ID NOs: 53, 55 or 57. In some embodiments, the mini-PCDH15 comprises two EC domains in the extracellular region (*e.g.*, any combination of two EC domains from among EC1, EC2, EC3, EC4, EC5, EC6, EC7, EC8, EC9, EC10 or EC11) of a full length PCDH15 extracellular domain set forth in SEQ ID NO: 1 or full length PCDH15 set forth in SEQ ID NOs: 53, 55 or 57. In some embodiments, the mini-PCDH15 comprises three EC domains in the extracellular region (*e.g.*, any combination of three EC domains from among EC1, EC2, EC3, EC4, EC5, EC6, EC7, EC8, EC9, EC10 or EC11) of a full length PCDH15 extracellular domain set forth in SEQ ID NO: 1 or full length PCDH15 set forth in SEQ ID NOs: 53, 55 or 57. In some embodiments, the mini-PCDH15 comprises four EC domains in the extracellular region (*e.g.*, any combination of four EC domains from among EC1, EC2, EC3, EC4, EC5, EC6, EC7, EC8, EC9, EC10 or EC11) of a full length PCDH15 extracellular domain set forth in SEQ ID NO: 1 or full length PCDH15 set forth in SEQ ID NOs: 53, 55 or 57. In some embodiments, the mini-PCDH15 comprises five EC domains in the extracellular region (*e.g.*, any combination of five EC domains from among EC1, EC2, EC3, EC4, EC5, EC6, EC7, EC8, EC9, EC10 or EC11) of a full length PCDH15 extracellular domain set forth in SEQ ID NO: 1 or full length PCDH15 set forth in SEQ ID NOs: 53, 55 or 57. In some embodiments, the mini-PCDH15 comprises six EC domains in the extracellular region (*e.g.*, any combination of six EC domains from among EC1, EC2, EC3, EC4, EC5, EC6, EC7, EC8, EC9, EC10 or EC11) of a full length PCDH15 extracellular domain set forth in SEQ ID NO: 1 or full length PCDH15

set forth in SEQ ID NOs: 53, 55 or 57. In some embodiments, the mini-PCDH15 comprises seven EC domains in the extracellular region (*e.g.*, any combination of seven EC domains from among EC1, EC2, EC3, EC4, EC5, EC6, EC7, EC8, EC9, EC10 or EC11) of a full length PCDH15 extracellular domain set forth in SEQ ID NO: 1 or full length PCDH15 set forth in SEQ ID NOs: 53, 55 or 57. In some embodiments, the mini-PCDH15 comprises eight EC domains in the extracellular region (*e.g.*, any combination of eight EC domains from among EC1, EC2, EC3, EC4, EC5, EC6, EC7, EC8, EC9, EC10 or EC11) of a full length PCDH15 extracellular domain set forth in SEQ ID NO: 1 or full length PCDH15 set forth in SEQ ID NOs: 53, 55 or 57. In some embodiments, the mini-PCDH15 comprises nine EC domains in the extracellular region (*e.g.*, any combination of nice EC domains from among EC1, EC2, EC3, EC4, EC5, EC6, EC7, EC8, EC9, EC10 or EC11) of a full length PCDH15 extracellular domain set forth in SEQ ID NO: 1 or full length PCDH15 set forth in SEQ ID NOs: 53, 55 or 57. In some embodiments, the mini-PCDH15 comprises ten EC domains in the extracellular region (*e.g.*, any combination of ten EC domains from among EC1, EC2, EC3, EC4, EC5, EC6, EC7, EC8, EC9, EC10 or EC11) of a full length PCDH15 extracellular domain set forth in SEQ ID NO: 1 or full length PCDH15 set forth in SEQ ID NOs: 53, 55 or 57.

As used herein, the term "sequence identity" refers to the percentage of amino acid (or nucleic acid) residues of a candidate sequence that are identical to the amino acid (or nucleic acid) residues of a reference sequence, *e.g.*, any of the mini-PCDH15 disclosed herein and their coding sequences, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent identity (*e.g.*, gaps can be introduced in one or both of the candidate and reference sequences for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). Alteration of the amino acid sequence or nucleic acid coding sequences can be obtained by deletion, addition or substitution of residues of the reference sequence. Alignment for purposes of determining percent identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software, such as BLAST, BLAST-2, BLAST-P, BLAST-N, BLAST-X, WU-BLAST-2, ALIGN, ALIGN-2, CLUSTAL, or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. For instance, the percent amino acid (or nucleic acid) sequence identity of a given candidate

sequence to, with, or against a given reference sequence (which can alternatively be phrased as a given candidate sequence that has or includes a certain percent amino acid (or nucleic acid) sequence identity to, with, or against a given reference sequence) is calculated as follows:

100 x (fraction of A/B)

where A is the number of amino acid (or nucleic acid) residues scored as identical in the alignment of the candidate sequence and the reference sequence, and where B is the total number of amino acid (or nucleic acid) residues in the reference sequence. In particular, a reference sequence aligned for comparison with a candidate sequence can show that the candidate sequence exhibits from, e.g., 50% to 100% identity across the full length of the candidate sequence or a selected portion of contiguous amino acid (or nucleic acid) residues of the candidate sequence. The length of the candidate sequence aligned for comparison purpose is at least 30%, e.g., at least 40%, e.g., at least 50%, 60%, 70%, 80%, 90%, or 100% of the length of the reference sequence. When a position in the candidate sequence is occupied by the same amino acid (or nucleic acid) residue as the corresponding position in the reference sequence, then the molecules are identical at that position.

In some embodiments, the mini-PCDH15 has 3 EC domains less than full-length PCDH15. In some examples, the mini-PCDH15 lacks EC4, EC7 and EC8 domain. In some embodiments, the mini-PCDH15 includes EC1-EC2-EC3-EC5-EC6-EC9-EC10-EC11 of SEQ ID NO: 1, 53, 55, or 57. In one example, the mini-PCDH15 comprises an amino acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 31, 75, or 76. In some embodiments, the nucleic acid encoding the mini-PCDH15 lacking EC4, EC7 and EC8 comprises a nucleic acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 32, 77, or 78.

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC7 and EC8 is set forth in SEQ ID NO: 31 (mini-PCDH15 V1: includes EC1-EC2-EC3-EC5-EC6-EC9-EC10-EC11-MAD12-TM-cyto CD1; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH

PLPAFAGLHIEILDENNQTPTFPEISYDVYVYTDMRPGDSVIQLTAVDADEGSNGEITYEILV
GAQGDFIINKTTGLITIAPGVEMIVGRTYALTVQAADNAPPAERRNSICTVYIEVLPPNNQ**SP**
PRFPQLMYSLEISEAMRVGAVLLNLQATDREGDSITYAIENGDPQRVFNLSETTGILTLGKAL
DRESTDRYILIITASDGRPDGTSTATVNIVVTDVNDNPPVFSKRIYKGMVAPDAVKGTPITTV
YAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSGRVITRVNLNEEPTTIFKLVVVAFDD
GEPVMSSSATVKILVLHPGE**IPRFTQEEYRPPPVSELATKGTMVGVISAAAINQSIVYSIVSG**
NEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSLEVVLANLRVPSKSNTAKVYIEIQDE
NNHPPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETY
TGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKK
IEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNEL
FKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GALLALAFIIILCCI**
PAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELG
DSSMHNLFLLYHFQQSRGNNSVSEDRKHQQVVMPFSSNTIEAHKSAHVDGSLKSNKLKSARKF
TFLSDEDDLSAHNPLYKENISQVSTNSDISQRTDFVDPFSPKIQAKSKSLRGPREKIQRLWSQ
SVSLPRRLMRKVPNRPEIIDLQQWQGTRQKAENENTGICTNKRGSSNPLLTTEEANLTEKEEI
RQGETLMIEGTEQLKSLSSDSSFCFPRPHFSFSTLPTVSRTVELKSEPNVISSPAECSLELSP
SRPCVLHSSLSRRETPICMLPIETERNIFENFAHPPNISPSACPLPPPPPISPPSPPPAPAPL
APPPDISPFSLFCPPPSPPSIPLPLPPPTFFPLSVSTSGPPTPPLLPPFPTPLPPPPPSIPCP
PPPSASFLSTECVCITGVKCTTNLMPAEKIKSSMTQLSTTTVCKTDPQREPKGILRHVKNLAE
LEKSVANMYSQIEKNYLRTNVSELQTMCPSEVTNMEITSEQNKGSLNNIVEGTEKQSHSQSTS
L (SEQ ID NO: 31)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC7 and EC8 is set forth in SEQ ID NO: 75 (mini-PCDH15 V1: includes EC1-EC2-EC3-EC5-EC6-EC9-EC10-EC11-MAD12-TM-cyto CD2; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQTPTFPEISYDVYVYTDMRPGDSVIQLTAVDADEGSNGEITYEILV
GAQGDFIINKTTGLITIAPGVEMIVGRTYALTVQAADNAPPAERRNSICTVYIEVLPPNNQ**SP**
PRFPQLMYSLEISEAMRVGAVLLNLQATDREGDSITYAIENGDPQRVFNLSETTGILTLGKAL
DRESTDRYILIITASDGRPDGTSTATVNIVVTDVNDNPPVFSKRIYKGMVAPDAVKGTPITTV
YAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSGRVITRVNLNEEPTTIFKLVVVAFDD
GEPVMSSSATVKILVLHPGE**IPRFTQEEYRPPPVSELATKGTMVGVISAAAINQSIVYSIVSG**
NEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSLEVVLANLRVPSKSNTAKVYIEIQDE
NNHPPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETY
TGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKK
IEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNEL
FKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GALLALAFIIILCCI**
PAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELG
DSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEEEPKKIKKPKVEIREPSEEEE
VVVTIEKPPAAEPTYTTWKRARIFPMIFKKVRGLADKRGIVDLEGEEWQRRLEEEDKDYLKLT
LDQEEATESTVESEEESSSDYTEYSEEESEFSESETTEEESESETPSEEEESSTPESEESEST

ESEGEKARKNIVLARRRPMVEEVKEVKGRKEEPQEEQKEPKMEEEEHSEEEESGPAPVEESTD PEAQDIPEEGSAESASVEGGVESEEESESGSSSSSSESQSGGPWGYQVPAYDRSKNANQKKSP GANSEGYNTAL (SEQ ID NO: 75)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC7 and EC8 is set forth in SEQ ID NO: 76 (mini-PCDH15 V1: includes EC1-EC2-EC3-EC5-EC6-EC9-EC10-EC11-MAD12-TM-cyto CD3; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI NKKVGTIIYHEVRIVVRDRNDN**SPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH PLPAFAGLHIEIL**DENNQ**TPTFPEISYDVYVYTDMRPGDSVIQLTAVDADEGSNGEITYEILV GAQGDFIINKTTGLITIAPGVEMIVGRTYALTVQAADNAPPAERRNSICTVYIEVLPPNNQ**SP PRFPQLMYSLEISEAMRVGAVLLNLQATDREGDSITYAIENGDPQRVFNLSETTGILTLGKAL DRESTDRYILIITASDGRPDGTSTATVNIVVT**DVNDN**PPVFSKRIYKGMVAPDAVKGTPITTV YAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSGRVITRVNLNEEPTTIFKLVVVAFDD GEPVMSSSATVKILVLHPGE**IPRFTQEEYRPPPVSELATKGTMVGVISAAAINQSIVYSIVSG NEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSLEVVLANLRVPSKSNTAKVYIEIQDE NNH**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETY TGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKK IEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNEL FKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GALLALAFIIILCCI PAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELG DSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEWARKRMIKLVVDREYETSSTG EDSAPECQRNRLHHPSIHSNINGNIYIAQNGSVVRTRRACLTDNLKVASPVRLGGPFKKLDKL AVTHEENVPLNTLSKGPFSTEKMNARPTLVTFAPCPVGTDNTAVKPLRNRLKSTVEQESMIDS KNIKEALEFHSDHTQSDDEELWMGPWNNLHIPMTKL** (SEQ ID NO: 76)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC7 and EC8 (V1) is set forth in SEQ ID NO: 32 (mini-PCDH15 V1: includes EC1-EC2-EC3-EC5-EC6-EC9-EC10-EC11-MAD12-TM-cyto CD1):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA

ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAACGCCAACC
TTCCCTGAAATATCCTATGATGTGTATGTTTATACAGACATGAGACCTGGGGACAGTGTCATA
CAGCTCACTGCAGTCGACGCAGACGAAGGGTCAAATGGGGAGATCACATATGAAATCCTTGTT
GGGGCTCAGGGAGACTTCATCATCAATAAAACAACAGGGCTTATCACCATCGCTCCAGGGGTG
GAAATGATAGTCGGGCGGACTTACGCACTCACGGTCCAAGCAGCGGATAATGCTCCTCCTGCA
GAGCGAAGGAACTCCATCTGCACTGTGTATATTGAAGTGCTTCCACCAAATAATCAAAGCCCT
CCTCGCTTCCCACAGCTGATGTATAGCCTTGAAATTAGTGAAGCCATGAGGGTTGGTGCTGTT
TTATTAAATCTACAGGCAACTGATCGAGAGGGAGACTCAATAACATATGCCATTGAGAATGGA
GATCCTCAGAGAGTTTTTAATCTTTCAGAAACCACGGGGATTCTAACCTTAGGGAAAGCACTG
GACAGGGAAAGCACTGATCGCTACATTCTGATCATCACAGCTTCAGATGGCAGGCCAGATGGG
ACCTCAACTGCCACAGTAAACATAGTGGTGACAGATGTCAATGACAATCCTCCTGTCTTTAGT
AAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTCAAGGGTACACCTATCACAACAGTT
TATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGTCGTGTGAGGTATAGAGTAGATGAT
GTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAAGAAGATTCTGGAAGAGTAATAACA
CGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAGTTGGTGGTGGTTGCTTTTGATGAT
GGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATTCTTGTCTTACATCCTGGTGAGATC
CCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTAAGTGAACTTGCCACCAAAGGGACC
ATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGTATTGTGTACTCCATTGTTTCAGGA
AATGAAGAAGATACATTTGGAATTAATAACATCACAGGTGTTATCTATGTGAATGGACCTCTG
GATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAAGCTGATTCCCTGGAAGTGGTCCTT
GCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAAGTATACATTGAGATTCAGGATGAA
AATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGA
ATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATG
GCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATAT
ACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAA
GTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTG
GTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAG
ATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTC
GTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAA
TGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTT
TTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAA
GGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAA
AGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATT
CCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACA
AAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCA
GTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGA
GACAGCTCAATGCATAATCTTTTCCTTCTCTACCATTTTCAACAAAGCAGGGGAAATAACTCA
GTCTCAGAAGACAGGAAACATCAACAAGTTGTGATGCCCTTTTCTTCCAATACTATTGAGGCT
CACAAGTCAGCTCATGTAGACGGATCACTTAAGAGCAACAAACTGAAGTCTGCAAGAAAATTC

ACATTTCTATCTGATGAGGATGACTTAAGTGCCCATAATCCCCTTTATAAGGAAAACATAAGT
CAAGTATCAACAAATTCAGACATTTCACAGAGAACAGATTTTGTAGACCCATTTTCACCCAAA
ATACAAGCCAAGAGTAAGTCTCTGAGGGGCCCAAGAGAAAAGATTCAGAGGCTGTGGAGTCAG
TCAGTCAGCTTACCCAGGAGGCTGATGAGGAAAGTTCCAAATAGACCAGAGATCATAGATCTG
CAGCAGTGGCAAGGCACCAGGCAGAAAGCTGAAAATGAAAACACTGGAATCTGTACAAACAAA
AGAGGTAGCAGCAATCCATTGCTTACAACTGAAGAGGCAAATTTGACAGAGAAAGAGGAAATA
AGGCAAGGTGAAACACTGATGATAGAAGGAACAGAACAGTTGAAATCTCTCTCTTCAGACTCT
TCATTTTGCTTTCCCAGGCCTCACTTCTCATTCTCCACTTTGCCAACTGTTTCAAGAACTGTG
GAACTCAAATCAGAACCTAATGTCATCAGTTCTCCTGCTGAGTGTTCCTTGGAACTTTCTCCT
TCAAGGCCTTGTGTTTTACATTCTTCACTCTCTAGGAGAGAGACACCTATTTGTATGTTACCT
ATTGAAACCGAAAGAAATATTTTTGAAAATTTTGCCCATCCACCAAACATCTCTCCTTCTGCC
TGTCCCCTTCCCCCTCCTCCTCCTATTTCTCCTCCTTCTCCTCCTCCTGCTCCTGCTCCTCTT
GCTCCTCCTCCTGACATTTCTCCTTTTTCTCTTTTTTGTCCTCCTCCCTCTCCTCCTTCTATC
CCTCTTCCTCTTCCTCCTCCTACATTTTTTCCACTTTCCGTTTCAACGTCTGGTCCCCCAACA
CCACCTCTTCTACCTCCATTTCCAACTCCTCTTCCTCCACCACCTCCTTCTATTCCTTGCCCT
CCACCTCCTTCAGCTTCATTTCTGTCCACAGAGTGTGTCTGTATAACAGGTGTTAAATGCACG
ACCAACTTGATGCCTGCCGAGAAAATTAAGTCCTCTATGACACAGCTATCAACAACGACAGTG
TGTAAAACAGACCCTCAGAGAGAACCAAAAGGCATCCTCAGACACGTTAAAAACTTAGCAGAA
CTTGAAAAATCAGTAGCTAACATGTACAGTCAAATAGAAAAAAACTATCTACGCACAAATGTT
TCAGAACTTCAAACTATGTGCCCTTCAGAAGTAACAAATATGGAAATCACATCTGAACAAAAC
AAGGGGAGTTTGAACAATATTGTCGAGGGAACTGAAAAACAATCTCACAGTCAATCTACTTCA
CTGTAA (SEQ ID NO: 32)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC7 and EC8 (V1) is set forth in SEQ ID NO: 77 (mini-PCDH15 V1: includes EC1-EC2-EC3-EC5-EC6-EC9-EC10-EC11-MAD12-TM-cyto CD2):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAACGCCAACC

TTCCCTGAAATATCCTATGATGTGTATGTTTATACAGACATGAGACCTGGGGACAGTGTCATA
CAGCTCACTGCAGTCGACGCAGACGAAGGGTCAAATGGGGAGATCACATATGAAATCCTTGTT
GGGGCTCAGGGAGACTTCATCATCAATAAAACAACAGGGCTTATCACCATCGCTCCAGGGGTG
GAAATGATAGTCGGGCGGACTTACGCACTCACGGTCCAAGCAGCGGATAATGCTCCTCCTGCA
GAGCGAAGGAACTCCATCTGCACTGTGTATATTGAAGTGCTTCCACCAAATAATCAAAGCCCT
CCTCGCTTCCCACAGCTGATGTATAGCCTTGAAATTAGTGAAGCCATGAGGGTTGGTGCTGTT
TTATTAAATCTACAGGCAACTGATCGAGAGGGAGACTCAATAACATATGCCATTGAGAATGGA
GATCCTCAGAGAGTTTTTAATCTTTCAGAAACCACGGGGATTCTAACCTTAGGGAAAGCACTG
GACAGGGAAAGCACTGATCGCTACATTCTGATCATCACAGCTTCAGATGGCAGGCCAGATGGG
ACCTCAACTGCCACAGTAAACATAGTGGTGACAGATGTCAATGACAATCCTCCTGTCTTTAGT
AAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTCAAGGGTACACCTATCACAACAGTT
TATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGTCGTGTGAGGTATAGAGTAGATGAT
GTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAAGAAGATTCTGGAAGAGTAATAACA
CGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAGTTGGTGGTGGTTGCTTTTGATGAT
GGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATTCTTGTCTTACATCCTGGTGAGATC
CCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTAAGTGAACTTGCCACCAAAGGGACC
ATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGTATTGTGTACTCCATTGTTTCAGGA
AATGAAGAAGATACATTTGGAATTAATAACATCACAGGTGTTATCTATGTGAATGGACCTCTG
GATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAAGCTGATTCCCTGGAAGTGGTCCTT
GCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAAGTATACATTGAGATTCAGGATGAA
AATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGA
ATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATG
GCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATAT
ACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAA
GTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTG
GTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAG
ATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTC
GTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAA
TGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTT
TTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAA
GGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAA
AGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATT
CCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACA
AAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCA
GTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGA
GACAGCTCAATGCATAAGTATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCA
GCTGGACAGGAGGAATATGGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAG
GAAGAGCCAAAGAAAATTAAAAAACCAAAGGTTGAAATTAGAGAGCCTAGTGAGGAGGAAGAA
GTAGTTGTAACTATCGAAAAACCACCAGCAGCTGAGCCTACATACACAACATGGAAGAGAGCC
AGAATATTCCCCATGATTTTTAAGAAAGTTAGAGGATTAGCTGATAAAAGAGGAATCGTTGAC
CTTGAGGGTGAAGAGTGGCAGAGACGCCTTGAGGAAGAAGATAAAGATTATTTGAAACTCACT
CTGGACCAAGAGGAAGCAACAGAAAGCACTGTAGAATCAGAGGAGGAATCCTCCAGCGACTAT
ACTGAATACAGTGAAGAAGAGTCTGAGTTCAGTGAGTCTGAGACTACAGAAGAGGAATCTGAG
TCAGAGACACCCTCTGAGGAGGAGGAGAGTTCCACCCCTGAATCAGAAGAATCGGAATCCACA
GAGTCAGAAGGAGAAAAAGCAAGGAAAAACATTGTGCTTGCAAGAAGAAGGCCCATGGTTGAG
GAGGTCAAGGAAGTCAAGGGTAGGAAAGAGGAGCCACAAGAAGAACAAAAAGAACCTAAGATG
GAAGAAGAAGAACACTCAGAAGAAGAAGAAAGTGGACCAGCCCCTGTGGAAGAAAGTACAGAC

CCTGAAGCTCAAGATATCCCTGAAGAGGGCAGTGCAGAATCAGCTTCGGTGGAAGGAGGTGTG
GAAAGTGAGGAGGAATCAGAATCAGGTAGTAGTAGCAGTAGTAGCGAAAGTCAGTCTGGAGGT
CCATGGGGCTATCAGGTACCAGCGTATGACAGAAGCAAGAATGCAAACCAAAAGAAGTCGCCA
GGAGCAAACTCTGAAGGTTACAACACAGCACTTTGA (SEQ ID NO: 77)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC7 and EC8 (V1) is set forth in SEQ ID NO: 78 (mini-PCDH15 V1: includes EC1-EC2-EC3-EC5-EC6-EC9-EC10-EC11-MAD12-TM-cyto CD3):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAACGCCAACC
TTCCCTGAAATATCCTATGATGTGTATGTTTATACAGACATGAGACCTGGGGACAGTGTCATA
CAGCTCACTGCAGTCGACGCAGACGAAGGGTCAAATGGGGAGATCACATATGAAATCCTTGTT
GGGGCTCAGGGAGACTTCATCATCAATAAAACAACAGGGCTTATCACCATCGCTCCAGGGGTG
GAAATGATAGTCGGGCGGACTTACGCACTCACGGTCCAAGCAGCGGATAATGCTCCTCCTGCA
GAGCGAAGGAACTCCATCTGCACTGTGTATATTGAAGTGCTTCCACCAAATAATCAAAGCCCT
CCTCGCTTCCCACAGCTGATGTATAGCCTTGAAATTAGTGAAGCCATGAGGGTTGGTGCTGTT
TTATTAAATCTACAGGCAACTGATCGAGAGGGAGACTCAATAACATATGCCATTGAGAATGGA
GATCCTCAGAGAGTTTTTAATCTTTCAGAAACCACGGGGATTCTAACCTTAGGGAAAGCACTG
GACAGGGAAAGCACTGATCGCTACATTCTGATCATCACAGCTTCAGATGGCAGGCCAGATGGG
ACCTCAACTGCCACAGTAAACATAGTGGTGACAGATGTCAATGACAATCCTCCTGTCTTTAGT
AAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTCAAGGGTACACCTATCACAACAGTT
TATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGTCGTGTGAGGTATAGAGTAGATGAT
GTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAAGAAGATTCTGGAAGAGTAATAACA
CGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAGTTGGTGGTGGTTGCTTTTGATGAT
GGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATTCTTGTCTTACATCCTGGTGAGATC
CCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTAAGTGAACTTGCCACCAAAGGGACC
ATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGTATTGTGTACTCCATTGTTTCAGGA
AATGAAGAAGATACATTTGGAATTAATAACATCACAGGTGTTATCTATGTGAATGGACCTCTG
GATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAAGCTGATTCCCTGGAAGTGGTCCTT

GCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAAGTATACATTGAGATTCAGGATGAA
AATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGA
ATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATG
GCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATAT
ACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAA
GTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTG
GTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAG
ATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTC
GTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAA
TGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTT
TTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAA
GGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAA
AGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATT
CCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACA
AAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCA
GTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGA
GACAGCTCAATGCATAAGTATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCA
GCTGGACAGGAGGAATATGGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAG
TGGGCAAGAAAAAGAATGATCAAGTTAGTTGTTGATCGAGAGTATGAAACCAGCTCAACTGGA
GAAGACAGTGCTCCTGAATGTCAGAGAAACCGTCTTCACCATCCTAGTATCCACAGTAATATC
AACGGCAATATATATATTGCACAGAATGGTTCTGTGGTGAGAACCCGCCGTGCCTGCCTCACG
GACAACTTAAAAGTTGCTTCCCCTGTTCGACTGGGAGGGCCCTTTAAGAAACTAGACAAGTTG
GCAGTGACACATGAGGAGAATGTACCTCTGAACACATTATCAAAGGGGCCATTTTCTACTGAA
AAAATGAATGCAAGACCAACTCTGGTTACATTTGCCCCTTGCCCTGTGGGGACTGACAATACA
GCGGTGAAGCCACTAAGGAACAGGCTGAAAAGCACAGTTGAACAGGAGTCCATGATTGACAGT
AAGAACATCAAGGAGGCTTTGGAATTTCATAGTGACCACACACAGTCTGATGATGAAGAGCTT
TGGATGGGCCCCTGGAACAACCTCCATATACCAATGACAAAACTGTGA (SEQ ID NO: 78)

In some examples, the mini-PCDH15 lacks EC5, EC6 and EC7 domain. In some embodiments, the mini-PCDH15 includes EC1-EC2-EC3-EC4-EC8-EC9-EC10-EC11 of SEQ ID NO: 1, 53, 55, or 57. In one example, the mini-PCDH15 comprises an amino acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 33, 79 or 80. In some embodiments, the nucleic acid encoding the mini-PCDH15 lacking EC5, EC6 and EC7 is at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 34, 81 or 82.

An exemplary amino acid sequence of a mini-PCDH15 lacking EC5, EC6 and EC7 (V2) is set forth in SEQ ID NO: 33 (mini-PCDH15 V2: includes EC1-EC2-EC3-EC4-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD1; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT
KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV
MDANDN**SPVFTNSTYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTG**
ELSLLRSLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDYPPVFSKRIYKGMV
APDAVKGTPITTVYAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSGRVITRVNLNEEP
TTIFKLVVVAFDDGEPVMSSSATVKILVLHPGE**IPRFTQEEYRPPPVSELATKGTMVGVISAA**
AINQSIVYSIVSGNEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSLEVVLANLRVPSK
SNTAKVYIEIQDENNHPPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPP
IKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQV
IVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAI
DPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GA**
LLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPP
PPPPGAHLYEELGDSSMHNLFLLYHFQQSRGNNSVSEDRKHQQVVMPFSSNTIEAHKSAHVDG
SLKSNKLKSARKFTFLSDEDDLSAHNPLYKENISQVSTNSDISQRTDFVDPFSPKIQAKSKSL
RGPREKIQRLWSQSVSLPRRLMRKVPNRPEIIDLQQWQGTRQKAENENTGICTNKRGSSNPLL
TTEEANLTEKEEIRQGETLMIEGTEQLKSLSSDSSFCFPRPHFSFSTLPTVSRTVELKSEPNV
ISSPAECSLELSPSRPCVLHSSLSRRETPICMLPIETERNIFENFAHPPNISPSACPLPPPPP
ISPPSPPPAPAPLAPPPDISPFSLFCPPPSPPSIPLPLPPPTFFPLSVSTSGPPTPPLLPPFP
TPLPPPPPSIPCPPPPSASFLSTECVCITGVKCTTNLMPAEKIKSSMTQLSTTTVCKTDPQRE
PKGILRHVKNLAELEKSVANMYSQIEKNYLRTNVSELQTMCPSEVTNMEITSEQNKGSLNNIV
EGTEKQSHSQSTSL (SEQ ID NO: 33)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC5, EC6 and EC7 (V2) is set forth in SEQ ID NO: 79 (mini-PCDH15 V2: includes EC1-EC2-EC3-EC4-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD2; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT
KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV
MDANDN**SPVFTNSTYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTG**
ELSLLRSLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDYPPVFSKRIYKGMV
APDAVKGTPITTVYAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSGRVITRVNLNEEP
TTIFKLVVVAFDDGEPVMSSSATVKILVLHPGE**IPRFTQEEYRPPPVSELATKGTMVGVISAA**
AINQSIVYSIVSGNEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSLEVVLANLRVPSK

SNTAKVYIEIQDENNHPPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPP
IKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQV
IVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAI
DPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GA**
LLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPP
PPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEEEPKKIKK
PKVEIREPSEEEEVVVTIEKPPAAEPTYTTWKRARIFPMIFKKVRGLADKRGIVDLEGEEWQR
RLEEEDKDYLKLTLDQEEATESTVESEEESSSDYTEYSEEESEFSESETTEEESESETPSEEE
ESSTPESEESESTESEGEKARKNIVLARRRPMVEEVKEVKGRKEEPQEEQKEPKMEEEEHSEE
EESGPAPVEESTDPEAQDIPEEGSAESASVEGGVESEEESESGSSSSSSESQSGGPWGYQVPA
YDRSKNANQKKSPGANSEGYNTAL (SEQ ID NO: 79)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC5, EC6 and EC7 (V2) is set forth in SEQ ID NO: 80 (mini-PCDH15 V2: includes EC1-EC2-EC3-EC4-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD3; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT
KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV
MDANDN**SPVFTNSTYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTG**
ELSLLRSLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDYPPVFSKRIYKGMV
APDAVKGTPITTVYAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSGRVITRVNLNEEP
TTIFKLVVVAFDDGEPVMSSSATVKILVLHPGE**IPRFTQEEYRPPPVSELATKGTMVGVISAA**
AINQSIVYSIVSGNEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSLEVVLANLRVPSK
SNTAKVYIEIQDENNHPPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPP
IKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQV
IVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAI
DPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GA**
LLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPP
PPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEWARKRMIK
LVVDREYETSSTGEDSAPECQRNRLHHPSIHSNINGNIYIAQNGSVVRTRRACLTDNLKVASP
VRLGGPFKKLDKLAVTHEENVPLNTLSKGPFSTEKMNARPTLVTFAPCPVGTDNTAVKPLRNR
LKSTVEQESMIDSKNIKEALEFHSDHTQSDDEELWMGPWNNLHIPMTKL (SEQ ID NO: 80)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC5, EC6 and EC7 (V2) is set forth in SEQ ID NO: 34 (mini-PCDH15 V2: includes EC1-EC2-EC3-EC4-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD1):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG
ATGGATGCAAATGATAACAGTCCTGTGTTCACCAATTCAACATACACTGTCCTTGTTGAAGAG
AATTTGCCAGCTGGGACTACCATCCTTCAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAAT
GTGTCTTACCGGATAAGAAGCCCAGAAGTGAAGCACTTTTTTGCACTACATCCATTTACAGGA
GAACTATCGCTTTTAAGGAGTTTAGATTATGAGGCATTTCCAGACCAAGAAGCAAGTATCACT
TTTCTGGTAGAGGCCTTTGATATTTATGGAACAATGCCACCTGGTATTGCTACTGTCACAGTG
ATTGTAAAGGATATGAATGATTATCCTCCTGTCTTTAGTAAACGAATATACAAAGGGATGGTG
GCTCCGGATGCAGTCAAGGGTACACCTATCACAACAGTTTATGCTGAAGATGCAGACCCTCCT
GGATTACCTGCAAGTCGTGTGAGGTATAGAGTAGATGATGTACAGTTTCCTTACCCTGCCAGT
ATTTTTGAAGTGGAAGAAGATTCTGGAAGAGTAATAACACGAGTCAATCTTAATGAAGAACCT
ACAACAATTTTTAAGTTGGTGGTGGTTGCTTTTGATGATGGGGAGCCTGTGATGTCCAGCAGT
GCCACAGTGAAGATTCTTGTCTTACATCCTGGTGAGATCCCACGCTTCACACAGGAGGAATAT
AGACCTCCTCCAGTAAGTGAACTTGCCACCAAAGGGACCATGGTTGGTGTAATTTCTGCTGCT
GCCATTAATCAAAGTATTGTGTACTCCATTGTTTCAGGAAATGAAGAAGATACATTTGGAATT
AATAACATCACAGGTGTTATCTATGTGAATGGACCTCTGGATTATGAGACCAGGACAAGCTAT
GTACTTCGAGTCCAAGCTGATTCCCTGGAAGTGGTCCTTGCCAATCTCCGAGTTCCTTCAAAA
AGCAATACAGCTAAAGTATACATTGAGATTCAGGATGAAAATAATCATCCCCCAGTGTTTCAG
AAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTG
AAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCA
ATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATG
CTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGG
AAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTC
ATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTG
GATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGC

CGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCAATT
GACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTA
CTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATCCGG
ACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCC
TTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTC
AGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCA
TTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCG
CCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAATCTTTTC
CTTCTCTACCATTTTCAACAAAGCAGGGGAAATAACTCAGTCTCAGAAGACAGGAAACATCAA
CAAGTTGTGATGCCCTTTTCTTCCAATACTATTGAGGCTCACAAGTCAGCTCATGTAGACGGA
TCACTTAAGAGCAACAAACTGAAGTCTGCAAGAAAATTCACATTTCTATCTGATGAGGATGAC
TTAAGTGCCCATAATCCCCTTTATAAGGAAAACATAAGTCAAGTATCAACAAATTCAGACATT
TCACAGAGAACAGATTTTGTAGACCCATTTTCACCCAAAATACAAGCCAAGAGTAAGTCTCTG
AGGGGCCCAAGAGAAAAGATTCAGAGGCTGTGGAGTCAGTCAGTCAGCTTACCCAGGAGGCTG
ATGAGGAAAGTTCCAAATAGACCAGAGATCATAGATCTGCAGCAGTGGCAAGGCACCAGGCAG
AAAGCTGAAAATGAAAACACTGGAATCTGTACAAACAAAAGAGGTAGCAGCAATCCATTGCTT
ACAACTGAAGAGGCAAATTTGACAGAGAAAGAGGAAATAAGGCAAGGTGAAACACTGATGATA
GAAGGAACAGAACAGTTGAAATCTCTCTCTTCAGACTCTTCATTTTGCTTTCCCAGGCCTCAC
TTCTCATTCTCCACTTTGCCAACTGTTTCAAGAACTGTGGAACTCAAATCAGAACCTAATGTC
ATCAGTTCTCCTGCTGAGTGTTCCTTGGAACTTTCTCCTTCAAGGCCTTGTGTTTTACATTCT
TCACTCTCTAGGAGAGAGACACCTATTTGTATGTTACCTATTGAAACCGAAAGAAATATTTTT
GAAAATTTTGCCCATCCACCAAACATCTCTCCTTCTGCCTGTCCCCTTCCCCCTCCTCCTCCT
ATTTCTCCTCCTTCTCCTCCTCCTGCTCCTGCTCCTCTTGCTCCTCCTCCTGACATTTCTCCT
TTTTCTCTTTTTTGTCCTCCTCCCTCTCCTCCTTCTATCCCTCTTCCTCTTCCTCCTCCTACA
TTTTTTCCACTTTCCGTTTCAACGTCTGGTCCCCCAACACCACCTCTTCTACCTCCATTTCCA
ACTCCTCTTCCTCCACCACCTCCTTCTATTCCTTGCCCTCCACCTCCTTCAGCTTCATTTCTG
TCCACAGAGTGTGTCTGTATAACAGGTGTTAAATGCACGACCAACTTGATGCCTGCCGAGAAA
ATTAAGTCCTCTATGACACAGCTATCAACAACGACAGTGTGTAAAACAGACCCTCAGAGAGAA
CCAAAAGGCATCCTCAGACACGTTAAAAACTTAGCAGAACTTGAAAAATCAGTAGCTAACATG
TACAGTCAAATAGAAAAAAACTATCTACGCACAAATGTTTCAGAACTTCAAACTATGTGCCCT
TCAGAAGTAACAAATATGGAAATCACATCTGAACAAAACAAGGGGAGTTTGAACAATATTGTC
GAGGGAACTGAAAAACAATCTCACAGTCAATCTACTTCACTGTAA (SEQ ID NO: 34)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC5, EC6 and EC7 (V2) is set forth in SEQ ID NO: 81 (mini-PCDH15 V2: includes EC1-EC2-EC3-EC4-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD2):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT

GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG
ATGGATGCAAATGATAACAGTCCTGTGTTCACCAATTCAACATACACTGTCCTTGTTGAAGAG
AATTTGCCAGCTGGGACTACCATCCTTCAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAAT
GTGTCTTACCGGATAAGAAGCCCAGAAGTGAAGCACTTTTTTGCACTACATCCATTTACAGGA
GAACTATCGCTTTTAAGGAGTTTAGATTATGAGGCATTTCCAGACCAAGAAGCAAGTATCACT
TTTCTGGTAGAGGCCTTTGATATTTATGGAACAATGCCACCTGGTATTGCTACTGTCACAGTG
ATTGTAAAGGATATGAATGATTATCCTCCTGTCTTTAGTAAACGAATATACAAAGGGATGGTG
GCTCCGGATGCAGTCAAGGGTACACCTATCACAACAGTTTATGCTGAAGATGCAGACCCTCCT
GGATTACCTGCAAGTCGTGTGAGGTATAGAGTAGATGATGTACAGTTTCCTTACCCTGCCAGT
ATTTTTGAAGTGGAAGAAGATTCTGGAAGAGTAATAACACGAGTCAATCTTAATGAAGAACCT
ACAACAATTTTTAAGTTGGTGGTGGTTGCTTTTGATGATGGGGAGCCTGTGATGTCCAGCAGT
GCCACAGTGAAGATTCTTGTCTTACATCCTGGTGAGATCCCACGCTTCACACAGGAGGAATAT
AGACCTCCTCCAGTAAGTGAACTTGCCACCAAAGGGACCATGGTTGGTGTAATTTCTGCTGCT
GCCATTAATCAAAGTATTGTGTACTCCATTGTTTCAGGAAATGAAGAAGATACATTTGGAATT
AATAACATCACAGGTGTTATCTATGTGAATGGACCTCTGGATTATGAGACCAGGACAAGCTAT
GTACTTCGAGTCCAAGCTGATTCCCTGGAAGTGGTCCTTGCCAATCTCCGAGTTCCTTCAAAA
AGCAATACAGCTAAAGTATACATTGAGATTCAGGATGAAAATAATCATCCCCCAGTGTTTCAG
AAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTG
AAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCA
ATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATG
CTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGG
AAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTC
ATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTG
GATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGC
CGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCAATT
GACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTA
CTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATCCGG
ACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCC
TTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTC
AGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCA
TTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCG
CCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAGTATGAA
ATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATATGGTGAG

GTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAGGAAGAGCCAAAGAAAATTAAAAAA
CCAAAGGTTGAAATTAGAGAGCCTAGTGAGGAGGAAGAAGTAGTTGTAACTATCGAAAAACCA
CCAGCAGCTGAGCCTACATACACAACATGGAAGAGAGCCAGAATATTCCCCATGATTTTTAAG
AAAGTTAGAGGATTAGCTGATAAAAGAGGAATCGTTGACCTTGAGGGTGAAGAGTGGCAGAGA
CGCCTTGAGGAAGAAGATAAAGATTATTTGAAACTCACTCTGGACCAAGAGGAAGCAACAGAA
AGCACTGTAGAATCAGAGGAGGAATCCTCCAGCGACTATACTGAATACAGTGAAGAAGAGTCT
GAGTTCAGTGAGTCTGAGACTACAGAAGAGGAATCTGAGTCAGAGACACCCTCTGAGGAGGAG
GAGAGTTCCACCCCTGAATCAGAAGAATCGGAATCCACAGAGTCAGAAGGAGAAAAAGCAAGG
AAAAACATTGTGCTTGCAAGAAGAAGGCCCATGGTTGAGGAGGTCAAGGAAGTCAAGGGTAGG
AAAGAGGAGCCACAAGAAGAACAAAAAGAACCTAAGATGGAAGAAGAAGAACACTCAGAAGAA
GAAGAAAGTGGACCAGCCCCTGTGGAAGAAAGTACAGACCCTGAAGCTCAAGATATCCCTGAA
GAGGGCAGTGCAGAATCAGCTTCGGTGGAAGGAGGTGTGGAAAGTGAGGAGGAATCAGAATCA
GGTAGTAGTAGCAGTAGTAGCGAAAGTCAGTCTGGAGGTCCATGGGGCTATCAGGTACCAGCG
TATGACAGAAGCAAGAATGCAAACCAAAAGAAGTCGCCAGGAGCAAACTCTGAAGGTTACAAC
ACAGCACTTTGA (SEQ ID NO: 81)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC5, EC6 and EC7 (V2) is set forth in SEQ ID NO: 82 (mini-PCDH15 V2: includes EC1-EC2-EC3-EC4-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD3):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG
ATGGATGCAAATGATAACAGTCCTGTGTTCACCAATTCAACATACACTGTCCTTGTTGAAGAG
AATTTGCCAGCTGGGACTACCATCCTTCAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAAT

GTGTCTTACCGGATAAGAAGCCCAGAAGTGAAGCACTTTTTTGCACTACATCCATTTACAGGA
GAACTATCGCTTTTAAGGAGTTTAGATTATGAGGCATTTCCAGACCAAGAAGCAAGTATCACT
TTTCTGGTAGAGGCCTTTGATATTTATGGAACAATGCCACCTGGTATTGCTACTGTCACAGTG
ATTGTAAAGGATATGAATGATTATCCTCCTGTCTTTAGTAAACGAATATACAAAGGGATGGTG
GCTCCGGATGCAGTCAAGGGTACACCTATCACAACAGTTTATGCTGAAGATGCAGACCCTCCT
GGATTACCTGCAAGTCGTGTGAGGTATAGAGTAGATGATGTACAGTTTCCTTACCCTGCCAGT
ATTTTTGAAGTGGAAGAAGATTCTGGAAGAGTAATAACACGAGTCAATCTTAATGAAGAACCT
ACAACAATTTTTAAGTTGGTGGTGGTTGCTTTTGATGATGGGGAGCCTGTGATGTCCAGCAGT
GCCACAGTGAAGATTCTTGTCTTACATCCTGGTGAGATCCCACGCTTCACACAGGAGGAATAT
AGACCTCCTCCAGTAAGTGAACTTGCCACCAAAGGGACCATGGTTGGTGTAATTTCTGCTGCT
GCCATTAATCAAAGTATTGTGTACTCCATTGTTTCAGGAAATGAAGAAGATACATTTGGAATT
AATAACATCACAGGTGTTATCTATGTGAATGGACCTCTGGATTATGAGACCAGGACAAGCTAT
GTACTTCGAGTCCAAGCTGATTCCCTGGAAGTGGTCCTTGCCAATCTCCGAGTTCCTTCAAAA
AGCAATACAGCTAAAGTATACATTGAGATTCAGGATGAAAATAATCATCCCCCAGTGTTTCAG
AAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTG
AAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCA
ATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATG
CTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGG
AAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTC
ATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTG
GATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGC
CGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCAATT
GACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTA
CTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATCCGG
ACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCC
TTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTC
AGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCA
TTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCG
CCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAGTATGAA
ATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATATGGTGAG
GTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAGTGGGCAAGAAAAAGAATGATCAAG
TTAGTTGTTGATCGAGAGTATGAAACCAGCTCAACTGGAGAAGACAGTGCTCCTGAATGTCAG
AGAAACCGTCTTCACCATCCTAGTATCCACAGTAATATCAACGGCAATATATATATTGCACAG
AATGGTTCTGTGGTGAGAACCCGCCGTGCCTGCCTCACGGACAACTTAAAAGTTGCTTCCCCT
GTTCGACTGGGAGGGCCCTTTAAGAAACTAGACAAGTTGGCAGTGACACATGAGGAGAATGTA
CCTCTGAACACATTATCAAAGGGGCCATTTTCTACTGAAAAAATGAATGCAAGACCAACTCTG
GTTACATTTGCCCCTTGCCCTGTGGGGACTGACAATACAGCGGTGAAGCCACTAAGGAACAGG
CTGAAAAGCACAGTTGAACAGGAGTCCATGATTGACAGTAAGAACATCAAGGAGGCTTTGGAA
TTTCATAGTGACCACACACAGTCTGATGATGAAGAGCTTTGGATGGGCCCCTGGAACAACCTC
CATATACCAATGACAAAACTGTGA (SEQ ID NO: 82)

In some embodiments, the mini-PCDH15 has 4 EC domains less than the full-length PCDH15. In some examples, the mini-PCDH15 lacks EC4, EC5, EC6 and EC7 domain. In some embodiments, the mini-PCDH15 includes EC1-EC2-EC3-EC8-EC9-EC10-EC11of SEQ ID NO: 1, 53, 55, or 57. In one example, the mini-PCDH15 comprises an amino acid sequence

at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 35, 83, or 84. In some embodiments, the nucleic acid encoding the mini-PCDH15 lacking EC4, EC5, EC6 and EC7 is at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 36, 85, or 86.

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC5, EC6 and EC7 (V3) is set forth in SEQ ID NO: 35 (mini-PCDH15 V3: includes EC1-EC2-EC3-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD1; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEIL<u>**DENNQ**</u>SPVFTNSTYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPE
VKHFFALHPFTGELSLLRSLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDY**P**
PVFSKRIYKGMVAPDAVKGTPITTVYAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSG
RVITRVNLNEEPTTIFKLVVVAFDDGEPVMSSSATVKILVLHPGEIPRFTQEEYRPPPVSELA
TKGTMVGVISAAAINQSIVYSIVSGNEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSL
EVVLANLRVPSKSNTAKVYIEIQDENNH**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGN**
YSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADV
LVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLE
DYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIK
KRGESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVP**
APAPVAAPPPPPPPPPGAHLYEELGDSSMHNLFLLYHFQQSRGNNSVSEDRKHQQVVMPFSSN
TIEAHKSAHVDGSLKSNKLKSARKFTFLSDEDDLSAHNPLYKENISQVSTNSDISQRTDFVDP
FSPKIQAKSKSLRGPREKIQRLWSQSVSLPRRLMRKVPNRPEIIDLQQWQGTRQKAENENTGI
CTNKRGSSNPLLTTEEANLTEKEEIRQGETLMIEGTEQLKSLSSDSSFCFPRPHFSFSTLPTV
SRTVELKSEPNVISSPAECSLELSPSRPCVLHSSLSRRETPICMLPIETERNIFENFAHPPNI
SPSACPLPPPPPISPPSPPPAPAPLAPPPDISPFSLFCPPPSPPSIPLPLPPPTFFPLSVSTS
GPPTPPLLPPFFPTPLPPPPPSIPCPPPPSASFLSTECVCITGVKCTTNLMPAEKIKSSMTQLS
TTTVCKTDPQREPKGILRHVKNLAELEKSVANMYSQIEKNYLRTNVSELQTMCPSEVTNMEIT
SEQNKGSLNNIVEGTEKQSHSQSTSL (SEQ ID NO: 35)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC5, EC6 and EC7 (V3) is set forth in SEQ ID NO: 83 (mini-PCDH15 V3: includes EC1-EC2-EC3-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD2; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPVFTNSTYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPE
VKHFFALHPFTGELSLLRSLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDY**P**
PVFSKRIYKGMVAPDAVKGTPITTVYAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSG
RVITRVNLNEEPTTIFKLVVVAFDDGEPVMSSSATVKILVLHPGEIPRFTQEEYRPPPVSELA
TKGTMVGVISAAAINQSIVYSIVSGNEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSL
EVVLANLRVPSKSNTAKVYIEIQDENNH**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGN**
YSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADV
LVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLE
DYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIK
KRGESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVP**
APAPVAAPPPPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEY
EEEEEEPKKIKKPKVEIREPSEEEEVVVTIEKPPAAEPTYTTWKRARIFPMIFKKVRGLADKR
GIVDLEGEEWQRRLEEEDKDYLKLTLDQEEATESTVESEEESSSDYTEYSEEESEFSESETTE
EESESETPSEEEESSTPESEESESTESEGEKARKNIVLARRRPMVEEVKEVKGRKEEPQEEQK
EPKMEEEEHSEEEESGPAPVEESTDPEAQDIPEEGSAESASVEGGVESEEESESGSSSSSSES
QSGGPWGYQVPAYDRSKNANQKKSPGANSEGYNTAL (SEQ ID NO: 83)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC5, EC6 and EC7 (V3) is set forth in SEQ ID NO: 84 (mini-PCDH15 V3: includes EC1-EC2-EC3-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD3; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPVFTNSTYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPE
VKHFFALHPFTGELSLLRSLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDY**P**
PVFSKRIYKGMVAPDAVKGTPITTVYAEDADPPGLPASRVRYRVDDVQFPYPASIFEVEEDSG
RVITRVNLNEEPTTIFKLVVVAFDDGEPVMSSSATVKILVLHPGEIPRFTQEEYRPPPVSELA
TKGTMVGVISAAAINQSIVYSIVSGNEEDTFGINNITGVIYVNGPLDYETRTSYVLRVQADSL
EVVLANLRVPSKSNTAKVYIEIQDENNH**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGN**
YSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADV
LVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLE
DYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIK
KRGESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVP**
APAPVAAPPPPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEY
EEEEWARKRMIKLVVDREYETSSTGEDSAPECQRNRLHHPSIHSNINGNIYIAQNGSVVRTRR

ACLTDNLKVASPVRLGGPFKKLDKLAVTHEENVPLNTLSKGPFSTEKMNARPTLVTFAPCPVG TDNTAVKPLRNRLKSTVEQESMIDSKNIKEALEFHSDHTQSDDEELWMGPWNNLHIPMTKL (SEQ ID NO: 84)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC5, EC6 and EC7 (V3) is set forth in SEQ ID NO: 36 (mini-PCDH15 V3: includes EC1-EC2-EC3-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD1):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCTGTG
TTCACCAATTCAACATACACTGTCCTTGTTGAAGAGAATTTGCCAGCTGGGACTACCATCCTT
CAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTACCGGATAAGAAGCCCAGAA
GTGAAGCACTTTTTTGCACTACATCCATTTACAGGAGAACTATCGCTTTTAAGGAGTTTAGAT
TATGAGGCATTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTAGAGGCCTTTGATATTTAT
GGAACAATGCCACCTGGTATTGCTACTGTCACAGTGATTGTAAAGGATATGAATGATTATCCT
CCTGTCTTTAGTAAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTCAAGGGTACACCT
ATCACAACAGTTTATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGTCGTGTGAGGTAT
AGAGTAGATGATGTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAAGAAGATTCTGGA
AGAGTAATAACACGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAGTTGGTGGTGGTT
GCTTTTGATGATGGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATTCTTGTCTTACAT
CCTGGTGAGATCCCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTAAGTGAACTTGCC
ACCAAAGGGACCATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGTATTGTGTACTCC
ATTGTTTCAGGAAATGAAGAAGATACATTTGGAATTAATAACATCACAGGTGTTATCTATGTG
AATGGACCTCTGGATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAAGCTGATTCCCTG
GAAGTGGTCCTTGCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAAGTATACATTGAG
ATTCAGGATGAAAATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCT
GAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAAT
TATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTA
GTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTAC

TTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTA
CTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTA
GTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCT
GGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAA
GATTACACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGAT
AGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCG
TATTATGGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAA
AAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATC
CTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAA
GCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCG
GCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTAT
GAAGAACTTGGAGACAGCTCAATGCATAATCTTTTCCTTCTCTACCATTTTCAACAAAGCAGG
GGAAATAACTCAGTCTCAGAAGACAGGAAACATCAACAAGTTGTGATGCCCTTTTCTTCCAAT
ACTATTGAGGCTCACAAGTCAGCTCATGTAGACGGATCACTTAAGAGCAACAAACTGAAGTCT
GCAAGAAAATTCACATTTCTATCTGATGAGGATGACTTAAGTGCCCATAATCCCCTTTATAAG
GAAAACATAAGTCAAGTATCAACAAATTCAGACATTTCACAGAGAACAGATTTTGTAGACCCA
TTTTCACCCAAAATACAAGCCAAGAGTAAGTCTCTGAGGGGCCCAAGAGAAAAGATTCAGAGG
CTGTGGAGTCAGTCAGTCAGCTTACCCAGGAGGCTGATGAGGAAAGTTCCAAATAGACCAGAG
ATCATAGATCTGCAGCAGTGGCAAGGCACCAGGCAGAAAGCTGAAAATGAAAACACTGGAATC
TGTACAAACAAAAGAGGTAGCAGCAATCCATTGCTTACAACTGAAGAGGCAAATTTGACAGAG
AAAGAGGAAATAAGGCAAGGTGAAACACTGATGATAGAAGGAACAGAACAGTTGAAATCTCTC
TCTTCAGACTCTTCATTTTGCTTTCCCAGGCCTCACTTCTCATTCTCCACTTTGCCAACTGTT
TCAAGAACTGTGGAACTCAAATCAGAACCTAATGTCATCAGTTCTCCTGCTGAGTGTTCCTTG
GAACTTTCTCCTTCAAGGCCTTGTGTTTTACATTCTTCACTCTCTAGGAGAGAGACACCTATT
TGTATGTTACCTATTGAAACCGAAAGAAATATTTTTGAAAATTTTGCCCATCCACCAAACATC
TCTCCTTCTGCCTGTCCCCTTCCCCCTCCTCCTCCTATTTCTCCTCCTTCTCCTCCTCCTGCT
CCTGCTCCTCTTGCTCCTCCTCCTGACATTTCTCCTTTTTCTCTTTTTTGTCCTCCTCCCTCT
CCTCCTTCTATCCCTCTTCCTCTTCCTCCTCCTACATTTTTTCCACTTTCCGTTTCAACGTCT
GGTCCCCCAACACCACCTCTTCTACCTCCATTTCCAACTCCTCTTCCTCCACCACCTCCTTCT
ATTCCTTGCCCTCCACCTCCTTCAGCTTCATTTCTGTCCACAGAGTGTGTCTGTATAACAGGT
GTTAAATGCACGACCAACTTGATGCCTGCCGAGAAAATTAAGTCCTCTATGACACAGCTATCA
ACAACGACAGTGTGTAAAACAGACCCTCAGAGAGAACCAAAAGGCATCCTCAGACACGTTAAA
AACTTAGCAGAACTTGAAAAATCAGTAGCTAACATGTACAGTCAAATAGAAAAAAACTATCTA
CGCACAAATGTTTCAGAACTTCAAACTATGTGCCCTTCAGAAGTAACAAATATGGAAATCACA
TCTGAACAAAACAAGGGGAGTTTGAACAATATTGTCGAGGGAACTGAAAAACAATCTCACAGT
CAATCTACTTCACTGTAA (SEQ ID NO: 36)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC5, EC6 and EC7 (V3) is set forth in SEQ ID NO: 85 (mini-PCDH15 V3: includes EC1-EC2-EC3-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD2):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA

AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCTGTG
TTCACCAATTCAACATACACTGTCCTTGTTGAAGAGAATTTGCCAGCTGGGACTACCATCCTT
CAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTACCGGATAAGAAGCCCAGAA
GTGAAGCACTTTTTTGCACTACATCCATTTACAGGAGAACTATCGCTTTTAAGGAGTTTAGAT
TATGAGGCATTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTAGAGGCCTTTGATATTTAT
GGAACAATGCCACCTGGTATTGCTACTGTCACAGTGATTGTAAAGGATATGAATGATTATCCT
CCTGTCTTTAGTAAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTCAAGGGTACACCT
ATCACAACAGTTTATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGTCGTGTGAGGTAT
AGAGTAGATGATGTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAAGAAGATTCTGGA
AGAGTAATAACACGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAGTTGGTGGTGGTT
GCTTTTGATGATGGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATTCTTGTCTTACAT
CCTGGTGAGATCCCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTAAGTGAACTTGCC
ACCAAAGGGACCATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGTATTGTGTACTCC
ATTGTTTCAGGAAATGAAGAAGATACATTTGGAATTAATAACATCACAGGTGTTATCTATGTG
AATGGACCTCTGGATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAAGCTGATTCCCTG
GAAGTGGTCCTTGCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAAGTATACATTGAG
ATTCAGGATGAAAATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCT
GAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAAT
TATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTA
GTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTAC
TTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTA
CTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTA
GTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCT
GGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAA
GATTACACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGAT
AGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCG
TATTATGGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAA
AAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATC
CTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAA
GCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCG
GCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTAT
GAAGAACTTGGAGACAGCTCAATGCATAAGTATGAAATGCCTCAATATGGGAGTCGCCGTCGA
TTGTTACCACCAGCTGGACAGGAGGAATATGGTGAGGTGGTTGGTGAAGCTGAGGAAGAATAT
GAGGAGGAAGAGGAAGAGCCAAAGAAAATTAAAAAACCAAAGGTTGAAATTAGAGAGCCTAGT

GAGGAGGAAGAAGTAGTTGTAACTATCGAAAAACCACCAGCAGCTGAGCCTACATACACAACA
TGGAAGAGAGCCAGAATATTCCCCATGATTTTTAAGAAAGTTAGAGGATTAGCTGATAAAAGA
GGAATCGTTGACCTTGAGGGTGAAGAGTGGCAGAGACGCCTTGAGGAAGAAGATAAAGATTAT
TTGAAACTCACTCTGGACCAAGAGGAAGCAACAGAAAGCACTGTAGAATCAGAGGAGGAATCC
TCCAGCGACTATACTGAATACAGTGAAGAAGAGTCTGAGTTCAGTGAGTCTGAGACTACAGAA
GAGGAATCTGAGTCAGAGACACCCTCTGAGGAGGAGGAGAGTTCCACCCCTGAATCAGAAGAA
TCGGAATCCACAGAGTCAGAAGGAGAAAAAGCAAGGAAAAACATTGTGCTTGCAAGAAGAAGG
CCCATGGTTGAGGAGGTCAAGGAAGTCAAGGGTAGGAAAGAGGAGCCACAAGAAGAACAAAAA
GAACCTAAGATGGAAGAAGAAGAACACTCAGAAGAAGAAGAAAGTGGACCAGCCCCTGTGGAA
GAAAGTACAGACCCTGAAGCTCAAGATATCCCTGAAGAGGGCAGTGCAGAATCAGCTTCGGTG
GAAGGAGGTGTGGAAAGTGAGGAGGAATCAGAATCAGGTAGTAGTAGCAGTAGTAGCGAAAGT
CAGTCTGGAGGTCCATGGGGCTATCAGGTACCAGCGTATGACAGAAGCAAGAATGCAAACCAA
AAGAAGTCGCCAGGAGCAAACTCTGAAGGTTACAACACAGCACTTTGA (SEQ ID NO: 85)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC5, EC6 and EC7 (V3) is set forth in SEQ ID NO: 86 (mini-PCDH15 V3: includes EC1-EC2-EC3-EC8-EC9-EC10-EC11-MAD12-TM-cyto CD3):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCTGTG
TTCACCAATTCAACATACACTGTCCTTGTTGAAGAGAATTTGCCAGCTGGGACTACCATCCTT
CAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTACCGGATAAGAAGCCCAGAA
GTGAAGCACTTTTTTGCACTACATCCATTTACAGGAGAACTATCGCTTTTAAGGAGTTTAGAT
TATGAGGCATTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTAGAGGCCTTTGATATTTAT
GGAACAATGCCACCTGGTATTGCTACTGTCACAGTGATTGTAAAGGATATGAATGATTATCCT
CCTGTCTTTAGTAAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTCAAGGGTACACCT
ATCACAACAGTTTATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGTCGTGTGAGGTAT
AGAGTAGATGATGTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAAGAAGATTCTGGA
AGAGTAATAACACGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAGTTGGTGGTGGTT

GCTTTTGATGATGGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATTCTTGTCTTACAT
CCTGGTGAGATCCCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTAAGTGAACTTGCC
ACCAAAGGGACCATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGTATTGTGTACTCC
ATTGTTTCAGGAAATGAAGAAGATACATTTGGAATTAATAACATCACAGGTGTTATCTATGTG
AATGGACCTCTGGATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAAGCTGATTCCCTG
GAAGTGGTCCTTGCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAAGTATACATTGAG
ATTCAGGATGAAAATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCT
GAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAAT
TATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTA
GTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTAC
TTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTA
CTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTA
GTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCT
GGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAA
GATTACACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGAT
AGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCG
TATTATGGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAA
AAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATC
CTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAA
GCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCG
GCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTAT
GAAGAACTTGGAGACAGCTCAATGCATAAGTATGAAATGCCTCAATATGGGAGTCGCCGTCGA
TTGTTACCACCAGCTGGACAGGAGGAATATGGTGAGGTGGTTGGTGAAGCTGAGGAAGAATAT
GAGGAGGAAGAGTGGGCAAGAAAAAGAATGATCAAGTTAGTTGTTGATCGAGAGTATGAAACC
AGCTCAACTGGAGAAGACAGTGCTCCTGAATGTCAGAGAAACCGTCTTCACCATCCTAGTATC
CACAGTAATATCAACGGCAATATATATATTGCACAGAATGGTTCTGTGGTGAGAACCCGCCGT
GCCTGCCTCACGGACAACTTAAAAGTTGCTTCCCCTGTTCGACTGGGAGGGCCCTTTAAGAAA
CTAGACAAGTTGGCAGTGACACATGAGGAGAATGTACCTCTGAACACATTATCAAAGGGGCCA
TTTTCTACTGAAAAAATGAATGCAAGACCAACTCTGGTTACATTTGCCCCTTGCCCTGTGGGG
ACTGACAATACAGCGGTGAAGCCACTAAGGAACAGGCTGAAAAGCACAGTTGAACAGGAGTCC
ATGATTGACAGTAAGAACATCAAGGAGGCTTTGGAATTTCATAGTGACCACACACAGTCTGAT
GATGAAGAGCTTTGGATGGGCCCCTGGAACAACCTCCATATACCAATGACAAAACTGTGA
(SEQ ID NO: 86)

In some examples, the mini-PCDH15 lacks EC4, EC8, EC9 and EC10 domain. In some embodiments, the mini-PCDH15 includes EC1-EC2-EC3-EC5-EC6-EC7-EC11of SEQ ID NO: 1, 53, 55, or 57. In one example, the mini-PCDH15 comprises an amino acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 37, 87, or 88. In some embodiments, the nucleic acid encoding the mini-PCDH15 lacking EC4, EC8, EC9 and EC10 is at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 38, 89 or 90.

A exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC8, EC9 and EC10 (V5) is set forth in SEQ ID NO: 37 (mini-PCDH15 V5: includes EC1-EC2-EC3-EC5-EC6-EC7-EC11-MAD12-TM-cyto CD1; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQTPTFPEISYDVYVYTDMRPGDSVIQLTAVDADEGSNGEITYEILV
GAQGDFIINKTTGLITIAPGVEMIVGRTYALTVQAADNAPPAERRNSICTVYIEVLPPNNQ**SP**
PRFPQLMYSLEISEAMRVGAVLLNLQATDREGDSITYAIENGDPQRVFNLSETTGILTLGKAL
DRESTDRYILIITASDGRPDGTSTATVNIVVTDVNDNAPVFDPYLPRNLSVVEEEANAFVGQV
KATDPDAGINGQVHYSLGNFNNLFRITSNGSIYTAVKLNREVRDYYELVVVATDGAVHPRHST
LTLAIKVLDIDDN**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKE**
GKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQVIVS
NVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAIDPQ
TNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GALLA**
LAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPP
PGAHLYEELGDSSMHNLFLLYHFQQSRGNNSVSEDRKHQQVVMPFSSNTIEAHKSAHVDGSLK
SNKLKSARKFTFLSDEDDLSAHNPLYKENISQVSTNSDISQRTDFVDPFSPKIQAKSKSLRGP
REKIQRLWSQSVSLPRRLMRKVPNRPEIIDLQQWQGTRQKAENENTGICTNKRGSSNPLLTTE
EANLTEKEEIRQGETLMIEGTEQLKSLSSDSSFCFPRPHFSFSTLPTVSRTVELKSEPNVISS
PAECSLELSPSRPCVLHSSLSRRETPICMLPIETERNIFENFAHPPNISPSACPLPPPPPISP
PSPPPAPAPLAPPPDISPFSLFCPPPSPPSIPLPLPPPTFFPLSVSTSGPPTPPLLPPFPTPL
PPPPPSIPCPPPPSASFLSTECVCITGVKCTTNLMPAEKIKSSMTQLSTTTVCKTDPQREPKG
ILRHVKNLAELEKSVANMYSQIEKNYLRTNVSELQTMCPSEVTNMEITSEQNKGSLNNIVEGT
EKQSHSQSTSL (SEQ ID NO: 37)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC8, EC9 and EC10 (V5) is set forth in SEQ ID NO: 87 (mini-PCDH15 V5: includes EC1-EC2-EC3-EC5-EC6-EC7-EC11-MAD12-TM-cyto CD2; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQTPTFPEISYDVYVYTDMRPGDSVIQLTAVDADEGSNGEITYEILV
GAQGDFIINKTTGLITIAPGVEMIVGRTYALTVQAADNAPPAERRNSICTVYIEVLPPNNQ**SP**
PRFPQLMYSLEISEAMRVGAVLLNLQATDREGDSITYAIENGDPQRVFNLSETTGILTLGKAL

DRESTDRYILIITASDGRPDGTSTATVNIVVTDVNDNAPVFDPYLPRNLSVVEEEANAFVGQV
KATDPDAGINGQVHYSLGNFNNLFRITSNGSIYTAVKLNREVRDYYELVVVATDGAVHPRHST
LTLAIKVLDIDDN**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKE**
GKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQVIVS
NVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAIDPQ
TNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GALLA**
LAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPP
PGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEEEPKKIKKPKV
EIREPSEEEEVVVTIEKPPAAEPTYTTWKRARIFPMIFKKVRGLADKRGIVDLEGEEWQRRLE
EEDKDYLKLTLDQEEATESTVESEEESSSDYTEYSEEESEFSESETTEEESESETPSEEEESS
TPESEESESTESEGEKARKNIVLARRRPMVEEVKEVKGRKEEPQEEQKEPKMEEEEHSEEEES
GPAPVEESTDPEAQDIPEEGSAESASVEGGVESEEESESGSSSSSSESQSGGPWGYQVPAYDR
SKNANQKKSPGANSEGYNTAL (SEQ ID NO: 87)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC8, EC9 and EC10 (V5) is set forth in SEQ ID NO: 88 (mini-PCDH15 V5: includes EC1-EC2-EC3-EC5-EC6-EC7-EC11-MAD12-TM-cyto CD3; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQTPTFPEISYDVYVYTDMRPGDSVIQLTAVDADEGSNGEITYEILV
GAQGDFIINKTTGLITIAPGVEMIVGRTYALTVQAADNAPPAERRNSICTVYIEVLPPNNQ**SP**
PRFPQLMYSLEISEAMRVGAVLLNLQATDREGDSITYAIENGDPQRVFNLSETTGILTLGKAL
DRESTDRYILIITASDGRPDGTSTATVNIVVTDVNDNAPVFDPYLPRNLSVVEEEANAFVGQV
KATDPDAGINGQVHYSLGNFNNLFRITSNGSIYTAVKLNREVRDYYELVVVATDGAVHPRHST
LTLAIKVLDIDDN**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKE**
GKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQVIVS
NVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAIDPQ
TNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GALLA**
LAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPP
PGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEWARKRMIKLVV
DREYETSSTGEDSAPECQRNRLHHPSIHSNINGNIYIAQNGSVVRTRRACLTDNLKVASPVRL
GGPFKKLDKLAVTHEENVPLNTLSKGPFSTEKMNARPTLVTFAPCPVGTDNTAVKPLRNRLKS
TVEQESMIDSKNIKEALEFHSDHTQSDDEELWMGPWNNLHIPMTKL (SEQ ID NO: 88)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC8, EC9 and EC10 (V5) is set forth in SEQ ID NO: 38 (mini-PCDH15 V5: includes EC1-EC2-EC3-EC5-EC6-EC7-EC11-MAD12-TM-cyto CD1):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAACGCCAACC
TTCCCTGAAATATCCTATGATGTGTATGTTTATACAGACATGAGACCTGGGGACAGTGTCATA
CAGCTCACTGCAGTCGACGCAGACGAAGGGTCAAATGGGGAGATCACATATGAAATCCTTGTT
GGGGCTCAGGGAGACTTCATCATCAATAAAACAACAGGGCTTATCACCATCGCTCCAGGGGTG
GAAATGATAGTCGGGCGGACTTACGCACTCACGGTCCAAGCAGCGGATAATGCTCCTCCTGCA
GAGCGAAGGAACTCCATCTGCACTGTGTATATTGAAGTGCTTCCACCAAATAATCAAAGCCCT
CCTCGCTTCCCACAGCTGATGTATAGCCTTGAAATTAGTGAAGCCATGAGGGTTGGTGCTGTT
TTATTAAATCTACAGGCAACTGATCGAGAGGGAGACTCAATAACATATGCCATTGAGAATGGA
GATCCTCAGAGAGTTTTTAATCTTTCAGAAACCACGGGGATTCTAACCTTAGGGAAAGCACTG
GACAGGGAAAGCACTGATCGCTACATTCTGATCATCACAGCTTCAGATGGCAGGCCAGATGGG
ACCTCAACTGCCACAGTAAACATAGTGGTGACAGATGTCAATGACAATGCTCCAGTGTTTGAT
CCTTATCTGCCAAGAAATTTATCTGTGGTGGAAGAAGAAGCCAATGCCTTTGTGGGTCAAGTA
AAAGCAACAGACCCTGATGCTGGAATAAATGGTCAAGTGCACTACAGTTTGGGTAACTTTAAT
AATCTTTTTCGTATCACATCCAATGGGAGCATTTACACAGCAGTGAAGCTTAACAGAGAAGTC
AGGGACTACTATGAACTTGTTGTTGTGGCAACAGATGGAGCAGTACACCCTCGTCATTCAACT
CTAACCTTGGCCATCAAGGTTTTGGACATTGATGATAACCCCCCAGTGTTTCAGAAAAAATTC
TACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACT
GATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAAGAG
GGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCAT
AATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTG
AGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCC
AATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTAT
GTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGA
GATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAA
ACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATC
AATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAG
GCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCT
CTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGA
CAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCG

GCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCG
CCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAATCTTTTCCTTCTCTAC
CATTTTCAACAAAGCAGGGGAAATAACTCAGTCTCAGAAGACAGGAAACATCAACAAGTTGTG
ATGCCCTTTTCTTCCAATACTATTGAGGCTCACAAGTCAGCTCATGTAGACGGATCACTTAAG
AGCAACAAACTGAAGTCTGCAAGAAAATTCACATTTCTATCTGATGAGGATGACTTAAGTGCC
CATAATCCCCTTTATAAGGAAAACATAAGTCAAGTATCAACAAATTCAGACATTTCACAGAGA
ACAGATTTTGTAGACCCATTTTCACCCAAAATACAAGCCAAGAGTAAGTCTCTGAGGGGCCCA
AGAGAAAAGATTCAGAGGCTGTGGAGTCAGTCAGTCAGCTTACCCAGGAGGCTGATGAGGAAA
GTTCCAAATAGACCAGAGATCATAGATCTGCAGCAGTGGCAAGGCACCAGGCAGAAAGCTGAA
AATGAAAACACTGGAATCTGTACAAACAAAAGAGGTAGCAGCAATCCATTGCTTACAACTGAA
GAGGCAAATTTGACAGAGAAAGAGGAAATAAGGCAAGGTGAAACACTGATGATAGAAGGAACA
GAACAGTTGAAATCTCTCTCTTCAGACTCTTCATTTTGCTTTCCCAGGCCTCACTTCTCATTC
TCCACTTTGCCAACTGTTTCAAGAACTGTGGAACTCAAATCAGAACCTAATGTCATCAGTTCT
CCTGCTGAGTGTTCCTTGGAACTTTCTCCTTCAAGGCCTTGTGTTTTACATTCTTCACTCTCT
AGGAGAGAGACACCTATTTGTATGTTACCTATTGAAACCGAAAGAAATATTTTTGAAAATTTT
GCCCATCCACCAAACATCTCTCCTTCTGCCTGTCCCCTTCCCCCTCCTCCTCCTATTTCTCCT
CCTTCTCCTCCTCCTGCTCCTGCTCCTCTTGCTCCTCCTCCTGACATTTCTCCTTTTTCTCTT
TTTTGTCCTCCTCCCTCTCCTCCTTCTATCCCTCTTCCTCTTCCTCCTCCTACATTTTTTCCA
CTTTCCGTTTCAACGTCTGGTCCCCCAACACCACCTCTTCTACCTCCATTTCCAACTCCTCTT
CCTCCACCACCTCCTTCTATTCCTTGCCCTCCACCTCCTTCAGCTTCATTTCTGTCCACAGAG
TGTGTCTGTATAACAGGTGTTAAATGCACGACCAACTTGATGCCTGCCGAGAAAATTAAGTCC
TCTATGACACAGCTATCAACAACGACAGTGTGTAAAACAGACCCTCAGAGAGAACCAAAAGGC
ATCCTCAGACACGTTAAAAACTTAGCAGAACTTGAAAAATCAGTAGCTAACATGTACAGTCAA
ATAGAAAAAAACTATCTACGCACAAATGTTTCAGAACTTCAAACTATGTGCCCTTCAGAAGTA
ACAAATATGGAAATCACATCTGAACAAAACAAGGGGAGTTTGAACAATATTGTCGAGGGAACT
GAAAAACAATCTCACAGTCAATCTACTTCACTGTAA (SEQ ID NO: 38)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC8, EC9 and EC10 (V5) is set forth in SEQ ID NO: 89 (mini-PCDH15 V5: includes EC1-EC2-EC3-EC5-EC6-EC7-EC11-MAD12-TM-cyto CD2):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC

CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAACGCCAACC
TTCCCTGAAATATCCTATGATGTGTATGTTTATACAGACATGAGACCTGGGGACAGTGTCATA
CAGCTCACTGCAGTCGACGCAGACGAAGGGTCAAATGGGGAGATCACATATGAAATCCTTGTT
GGGGCTCAGGGAGACTTCATCATCAATAAAACAACAGGGCTTATCACCATCGCTCCAGGGGTG
GAAATGATAGTCGGGCGGACTTACGCACTCACGGTCCAAGCAGCGGATAATGCTCCTCCTGCA
GAGCGAAGGAACTCCATCTGCACTGTGTATATTGAAGTGCTTCCACCAAATAATCAAAGCCCT
CCTCGCTTCCCACAGCTGATGTATAGCCTTGAAATTAGTGAAGCCATGAGGGTTGGTGCTGTT
TTATTAAATCTACAGGCAACTGATCGAGAGGGAGACTCAATAACATATGCCATTGAGAATGGA
GATCCTCAGAGAGTTTTTAATCTTTCAGAAACCACGGGGATTCTAACCTTAGGGAAAGCACTG
GACAGGGAAAGCACTGATCGCTACATTCTGATCATCACAGCTTCAGATGGCAGGCCAGATGGG
ACCTCAACTGCCACAGTAAACATAGTGGTGACAGATGTCAATGACAATGCTCCAGTGTTTGAT
CCTTATCTGCCAAGAAATTTATCTGTGGTGGAAGAAGAAGCCAATGCCTTTGTGGGTCAAGTA
AAAGCAACAGACCCTGATGCTGGAATAAATGGTCAAGTGCACTACAGTTTGGGTAACTTTAAT
AATCTTTTTCGTATCACATCCAATGGGAGCATTTACACAGCAGTGAAGCTTAACAGAGAAGTC
AGGGACTACTATGAACTTGTTGTTGTGGCAACAGATGGAGCAGTACACCCTCGTCATTCAACT
CTAACCTTGGCCATCAAGGTTTTGGACATTGATGATAACCCCCCAGTGTTTCAGAAAAAATTC
TACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACT
GATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAAGAG
GGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCAT
AATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTG
AGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCC
AATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTAT
GTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGA
GATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAA
ACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATC
AATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAG
GCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCT
CTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGA
CAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCG
GCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCG
CCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAGTATGAAATGCCTCAA
TATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATATGGTGAGGTGGTTGGT
GAAGCTGAGGAAGAATATGAGGAGGAAGAGGAAGAGCCAAAGAAAATTAAAAAACCAAAGGTT
GAAATTAGAGAGCCTAGTGAGGAGGAAGAAGTAGTTGTAACTATCGAAAAACCACCAGCAGCT
GAGCCTACATACACAACATGGAAGAGAGCCAGAATATTCCCCATGATTTTTAAGAAAGTTAGA
GGATTAGCTGATAAAAGAGGAATCGTTGACCTTGAGGGTGAAGAGTGGCAGAGACGCCTTGAG
GAAGAAGATAAAGATTATTTGAAACTCACTCTGGACCAAGAGGAAGCAACAGAAAGCACTGTA
GAATCAGAGGAGGAATCCTCCAGCGACTATACTGAATACAGTGAAGAAGAGTCTGAGTTCAGT
GAGTCTGAGACTACAGAAGAGGAATCTGAGTCAGAGACACCCTCTGAGGAGGAGGAGAGTTCC
ACCCCTGAATCAGAAGAATCGGAATCCACAGAGTCAGAAGGAGAAAAAGCAAGGAAAAACATT
GTGCTTGCAAGAAGAAGGCCCATGGTTGAGGAGGTCAAGGAAGTCAAGGGTAGGAAAGAGGAG
CCACAAGAAGAACAAAAAGAACCTAAGATGGAAGAAGAAGAACACTCAGAAGAAGAAGAAAGT
GGACCAGCCCCTGTGGAAGAAAGTACAGACCCTGAAGCTCAAGATATCCCTGAAGAGGGCAGT
GCAGAATCAGCTTCGGTGGAAGGAGGTGTGGAAAGTGAGGAGGAATCAGAATCAGGTAGTAGT

AGCAGTAGTAGCGAAAGTCAGTCTGGAGGTCCATGGGGCTATCAGGTACCAGCGTATGACAGA
AGCAAGAATGCAAACCAAAAGAAGTCGCCAGGAGCAAACTCTGAAGGTTACAACACAGCACTT
TGA (SEQ ID NO: 89)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC8, EC9 and EC10 (V5) is set forth in SEQ ID NO: 90 (mini-PCDH15 V5: includes EC1-EC2-EC3-EC5-EC6-EC7-EC11-MAD12-TM-cyto CD3):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAACGCCAACC
TTCCCTGAAATATCCTATGATGTGTATGTTTATACAGACATGAGACCTGGGGACAGTGTCATA
CAGCTCACTGCAGTCGACGCAGACGAAGGGTCAAATGGGGAGATCACATATGAAATCCTTGTT
GGGGCTCAGGGAGACTTCATCATCAATAAAACAACAGGGCTTATCACCATCGCTCCAGGGGTG
GAAATGATAGTCGGGCGGACTTACGCACTCACGGTCCAAGCAGCGGATAATGCTCCTCCTGCA
GAGCGAAGGAACTCCATCTGCACTGTGTATATTGAAGTGCTTCCACCAAATAATCAAAGCCCT
CCTCGCTTCCCACAGCTGATGTATAGCCTTGAAATTAGTGAAGCCATGAGGGTTGGTGCTGTT
TTATTAAATCTACAGGCAACTGATCGAGAGGGAGACTCAATAACATATGCCATTGAGAATGGA
GATCCTCAGAGAGTTTTTAATCTTTCAGAAACCACGGGGATTCTAACCTTAGGGAAAGCACTG
GACAGGGAAAGCACTGATCGCTACATTCTGATCATCACAGCTTCAGATGGCAGGCCAGATGGG
ACCTCAACTGCCACAGTAAACATAGTGGTGACAGATGTCAATGACAATGCTCCAGTGTTTGAT
CCTTATCTGCCAAGAAATTTATCTGTGGTGGAAGAAGAAGCCAATGCCTTTGTGGGTCAAGTA
AAAGCAACAGACCCTGATGCTGGAATAAATGGTCAAGTGCACTACAGTTTGGGTAACTTTAAT
AATCTTTTTCGTATCACATCCAATGGGAGCATTTACACAGCAGTGAAGCTTAACAGAGAAGTC
AGGGACTACTATGAACTTGTTGTTGTGGCAACAGATGGAGCAGTACACCCTCGTCATTCAACT
CTAACCTTGGCCATCAAGGTTTTGGACATTGATGATAACCCCCCAGTGTTTCAGAAAAAATTC
TACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACT
GATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAAGAG
GGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCAT
AATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTG

AGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCC
AATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTAT
GTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGA
GATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAA
ACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATC
AATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAG
GCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCT
CTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGA
CAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCG
GCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCG
CCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAGTATGAAATGCCTCAA
TATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATATGGTGAGGTGGTTGGT
GAAGCTGAGGAAGAATATGAGGAGGAAGAGTGGGCAAGAAAAAGAATGATCAAGTTAGTTGTT
GATCGAGAGTATGAAACCAGCTCAACTGGAGAAGACAGTGCTCCTGAATGTCAGAGAAACCGT
CTTCACCATCCTAGTATCCACAGTAATATCAACGGCAATATATATATTGCACAGAATGGTTCT
GTGGTGAGAACCCGCCGTGCCTGCCTCACGGACAACTTAAAAGTTGCTTCCCCTGTTCGACTG
GGAGGGCCCTTTAAGAAACTAGACAAGTTGGCAGTGACACATGAGGAGAATGTACCTCTGAAC
ACATTATCAAAGGGGCCATTTTCTACTGAAAAAATGAATGCAAGACCAACTCTGGTTACATTT
GCCCCTTGCCCTGTGGGGACTGACAATACAGCGGTGAAGCCACTAAGGAACAGGCTGAAAAGC
ACAGTTGAACAGGAGTCCATGATTGACAGTAAGAACATCAAGGAGGCTTTGGAATTTCATAGT
GACCACACACAGTCTGATGATGAAGAGCTTTGGATGGGCCCCTGGAACAACCTCCATATACCA
ATGACAAAACTGTGA (SEQ ID NO: 90)

In some examples, the mini-PCDH15 lacks EC5, EC6, EC9 and EC10 domain. In some embodiments, the mini-PCDH15 includes EC1-EC2-EC3-EC4-EC7-EC8-EC11 of SEQ ID NO: 1, 53, 55, or 57. In one example, the mini-PCDH15 comprises an amino acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 39, 91, or 92. In some embodiments, the nucleic acid encoding the mini-PCDH15 lacking EC5, EC6, EC9 and EC10 is at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 40, 93, or 94.

An exemplary amino acid sequence of a mini-PCDH15 lacking EC5, EC6, EC9 and EC10 (V6) is set forth in SEQ ID NO: 39 (mini-PCDH15 V6: includes EC1-EC2-EC3-EC4--EC7-EC8-EC11-MAD12-TM-cyto CD1; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**

RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT
KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV
MDANDN**APVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQVHYSLGNFNNLFRITSNGS**
IYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDDNSPVFTNSTYTVLVEENLP
AGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTGELSLLRSLDYEAFPDQEASITFLV
EAFDIYGTMPPGIATVTVIVKDMNDY**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYS**
VMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLV
SVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDY
TKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKR
GESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAP**
APVAAPPPPPPPPPGAHLYEELGDSSMHNLFLLYHFQQSRGNNSVSEDRKHQQVVMPFSSNTI
EAHKSAHVDGSLKSNKLKSARKFTFLSDEDDLSAHNPLYKENISQVSTNSDISQRTDFVDPFS
PKIQAKSKSLRGPREKIQRLWSQSVSLPRRLMRKVPNRPEIIDLQQWQGTRQKAENENTGICT
NKRGSSNPLLTTEEANLTEKEEIRQGETLMIEGTEQLKSLSSDSSFCFPRPHFSFSTLPTVSR
TVELKSEPNVISSPAECSLELSPSRPCVLHSSLSRRETPICMLPIETERNIFENFAHPPNISP
SACPLPPPPPISPPSPPPAPAPLAPPPDISPFSLFCPPPSPPSIPLPLPPPTFFPLSVSTSGP
PTPPLLPPFPTPLPPPPPSIPCPPPPSASFLSTECVCITGVKCTTNLMPAEKIKSSMTQLSTT
TVCKTDPQREPKGILRHVKNLAELEKSVANMYSQIEKNYLRTNVSELQTMCPSEVTNMEITSE
QNKGSLNNIVEGTEKQSHSQSTSL (SEQ ID NO: 39)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC5, EC6, EC9 and EC10 (V6) is set forth in SEQ ID NO: 91 (mini-PCDH15 V6: includes EC1-EC2-EC3-EC4--EC7-EC8-EC11-MAD12-TM-cyto CD2; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT
KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV
MDANDN**APVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQVHYSLGNFNNLFRITSNGS**
IYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDDNSPVFTNSTYTVLVEENLP
AGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTGELSLLRSLDYEAFPDQEASITFLV
EAFDIYGTMPPGIATVTVIVKDMNDY**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYS**
VMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLV
SVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDY
TKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKR
GESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAP**
APVAAPPPPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEE
EEEEPKKIKKPKVEIREPSEEEEVVVTIEKPPAAEPTYTTWKRARIFPMIFKKVRGLADKRGI
VDLEGEEWQRRLEEEDKDYLKLTLDQEEATESTVESEEESSSDYTEYSEEESEFSESETTEEE
SESETPSEEEESSTPESEESESTESEGEKARKNIVLARRRPMVEEVKEVKGRKEEPQEEQKEP

KMEEEEHSEEEESGPAPVEESTDPEAQDIPEEGSAESASVEGGVESEEESESGSSSSSSESQS GGPWGYQVPAYDRSKNANQKKSPGANSEGYNTAL (SEQ ID NO: 91)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC5, EC6, EC9 and EC10 (V6) is set forth in SEQ ID NO: 92 (mini-PCDH15 V6: includes EC1-EC2-EC3-EC4--EC7-EC8-EC11-MAD12-TM-cyto CD3; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI NKKVGTIIYHEVRIVVRDRNDN**SPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH PLPAFAGLHIEILDENNQ**SPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV MDANDN**APVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQVHYSLGNFNNLFRITSNGS IYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDDN**SPVFTNSTYTVLVEENLP AGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTGELSLLRSLDYEAFPDQEASITFLV EAFDIYGTMPPGIATVTVIVKDMNDY**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYS VMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLV SVVNQLD**MQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDY TKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKR GESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAP APVAAPPPPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEE EEWARKRMIKLVVDREYETSSTGEDSAPECQRNRLHHPSIHSNINGNIYIAQNGSVVRTRRAC LTDNLKVASPVRLGGPFKKLDKLAVTHEENVPLNTLSKGPFSTEKMNARPTLVTFAPCPVGTD NTAVKPLRNRLKSTVEQESMIDSKNIKEALEFHSDHTQSDDEELWMGPWNNLHIPMTKL** (SEQ ID NO: 92)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC5, EC6, EC9 and EC10 (V6) is set forth in SEQ ID NO: 40 (mini-PCDH15 V6: includes EC1-EC2-EC3-EC4--EC7-EC8-EC11-MAD12-TM-cyto CD1):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA

ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG
ATGGATGCAAATGATAACGCTCCAGTGTTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTG
GAAGAAGAAGCCAATGCCTTTGTGGGTCAAGTAAAAGCAACAGACCCTGATGCTGGAATAAAT
GGTCAAGTGCACTACAGTTTGGGTAACTTTAATAATCTTTTTCGTATCACATCCAATGGGAGC
ATTTACACAGCAGTGAAGCTTAACAGAGAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCA
ACAGATGGAGCAGTACACCCTCGTCATTCAACTCTAACCTTGGCCATCAAGGTTTTGGACATT
GATGATAACAGTCCTGTGTTCACCAATTCAACATACACTGTCCTTGTTGAAGAGAATTTGCCA
GCTGGGACTACCATCCTTCAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTAC
CGGATAAGAAGCCCAGAAGTGAAGCACTTTTTTGCACTACATCCATTTACAGGAGAACTATCG
CTTTTAAGGAGTTTAGATTATGAGGCATTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTA
GAGGCCTTTGATATTTATGGAACAATGCCACCTGGTATTGCTACTGTCACAGTGATTGTAAAG
GATATGAATGATTATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGAT
GCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGT
GTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAA
ACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAG
TTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTC
TCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAA
AAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCC
AAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTAC
ACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAAT
GAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTAT
GGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGA
GGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGC
TGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAG
TGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCT
GCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAA
CTTGGAGACAGCTCAATGCATAATCTTTTCCTTCTCTACCATTTTCAACAAAGCAGGGGAAAT
AACTCAGTCTCAGAAGACAGGAAACATCAACAAGTTGTGATGCCCTTTTCTTCCAATACTATT
GAGGCTCACAAGTCAGCTCATGTAGACGGATCACTTAAGAGCAACAAACTGAAGTCTGCAAGA
AAATTCACATTTCTATCTGATGAGGATGACTTAAGTGCCCATAATCCCCTTTATAAGGAAAAC
ATAAGTCAAGTATCAACAAATTCAGACATTTCACAGAGAACAGATTTTGTAGACCCATTTTCA
CCCAAAATACAAGCCAAGAGTAAGTCTCTGAGGGGCCCAAGAGAAAAGATTCAGAGGCTGTGG
AGTCAGTCAGTCAGCTTACCCAGGAGGCTGATGAGGAAAGTTCCAAATAGACCAGAGATCATA
GATCTGCAGCAGTGGCAAGGCACCAGGCAGAAAGCTGAAAATGAAAACACTGGAATCTGTACA

AACAAAAGAGGTAGCAGCAATCCATTGCTTACAACTGAAGAGGCAAATTTGACAGAGAAAGAG
GAAATAAGGCAAGGTGAAACACTGATGATAGAAGGAACAGAACAGTTGAAATCTCTCTCTTCA
GACTCTTCATTTTGCTTTCCCAGGCCTCACTTCTCATTCTCCACTTTGCCAACTGTTTCAAGA
ACTGTGGAACTCAAATCAGAACCTAATGTCATCAGTTCTCCTGCTGAGTGTTCCTTGGAACTT
TCTCCTTCAAGGCCTTGTGTTTTACATTCTTCACTCTCTAGGAGAGAGACACCTATTTGTATG
TTACCTATTGAAACCGAAAGAAATATTTTTGAAAATTTTGCCCATCCACCAAACATCTCTCCT
TCTGCCTGTCCCCTTCCCCCTCCTCCTCCTATTTCTCCTCCTTCTCCTCCTCCTGCTCCTGCT
CCTCTTGCTCCTCCTCCTGACATTTCTCCTTTTTTCTCTTTTTTTGTCCTCCTCCCTCTCCTCCT
TCTATCCCTCTTCCTCTTCCTCCTCCTACATTTTTTCCACTTTCCGTTTCAACGTCTGGTCCC
CCAACACCACCTCTTCTACCTCCATTTCCAACTCCTCTTCCTCCACCACCTCCTTCTATTCCT
TGCCCTCCACCTCCTTCAGCTTCATTTCTGTCCACAGAGTGTGTCTGTATAACAGGTGTTAAA
TGCACGACCAACTTGATGCCTGCCGAGAAAATTAAGTCCTCTATGACACAGCTATCAACAACG
ACAGTGTGTAAAACAGACCCTCAGAGAGAACCAAAAGGCATCCTCAGACACGTTAAAAACTTA
GCAGAACTTGAAAAATCAGTAGCTAACATGTACAGTCAAATAGAAAAAAACTATCTACGCACA
AATGTTTCAGAACTTCAAACTATGTGCCCTTCAGAAGTAACAAATATGGAAATCACATCTGAA
CAAAACAAGGGGAGTTTGAACAATATTGTCGAGGGAACTGAAAAACAATCTCACAGTCAATCT
ACTTCACTGTAA (SEQ ID NO: 40)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC5, EC6, EC9 and EC10 (V6) is set forth in SEQ ID NO: 93 (mini-PCDH15 V6: includes EC1-EC2-EC3-EC4--EC7-EC8-EC11-MAD12-TM-cyto CD2):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG

ATGGATGCAAATGATAACGCTCCAGTGTTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTG
GAAGAAGAAGCCAATGCCTTTGTGGGTCAAGTAAAAGCAACAGACCCTGATGCTGGAATAAAT
GGTCAAGTGCACTACAGTTTGGGTAACTTTAATAATCTTTTTCGTATCACATCCAATGGGAGC
ATTTACACAGCAGTGAAGCTTAACAGAGAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCA
ACAGATGGAGCAGTACACCCTCGTCATTCAACTCTAACCTTGGCCATCAAGGTTTTGGACATT
GATGATAACAGTCCTGTGTTCACCAATTCAACATACACTGTCCTTGTTGAAGAGAATTTGCCA
GCTGGGACTACCATCCTTCAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTAC
CGGATAAGAAGCCCAGAAGTGAAGCACTTTTTTGCACTACATCCATTTACAGGAGAACTATCG
CTTTTAAGGAGTTTAGATTATGAGGCATTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTA
GAGGCCTTTGATATTTATGGAACAATGCCACCTGGTATTGCTACTGTCACAGTGATTGTAAAG
GATATGAATGATTATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGAT
GCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGT
GTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAA
ACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAG
TTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTC
TCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAA
AAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCC
AAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTAC
ACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAAT
GAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTAT
GGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGA
GGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGC
TGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAG
TGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCT
GCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAA
CTTGGAGACAGCTCAATGCATAAGTATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTA
CCACCAGCTGGACAGGAGGAATATGGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAG
GAAGAGGAAGAGCCAAAGAAAATTAAAAAACCAAAGGTTGAAATTAGAGAGCCTAGTGAGGAG
GAAGAAGTAGTTGTAACTATCGAAAAACCACCAGCAGCTGAGCCTACATACACAACATGGAAG
AGAGCCAGAATATTCCCCATGATTTTTAAGAAAGTTAGAGGATTAGCTGATAAAAGAGGAATC
GTTGACCTTGAGGGTGAAGAGTGGCAGAGACGCCTTGAGGAAGAAGATAAAGATTATTTGAAA
CTCACTCTGGACCAAGAGGAAGCAACAGAAAGCACTGTAGAATCAGAGGAGGAATCCTCCAGC
GACTATACTGAATACAGTGAAGAAGAGTCTGAGTTCAGTGAGTCTGAGACTACAGAAGAGGAA
TCTGAGTCAGAGACACCCTCTGAGGAGGAGGAGAGTTCCACCCCTGAATCAGAAGAATCGGAA
TCCACAGAGTCAGAAGGAGAAAAAGCAAGGAAAAACATTGTGCTTGCAAGAAGAAGGCCCATG
GTTGAGGAGGTCAAGGAAGTCAAGGGTAGGAAAGAGGAGCCACAAGAAGAACAAAAAGAACCT
AAGATGGAAGAAGAAGAACACTCAGAAGAAGAAGAAAGTGGACCAGCCCCTGTGGAAGAAAGT
ACAGACCCTGAAGCTCAAGATATCCCTGAAGAGGGCAGTGCAGAATCAGCTTCGGTGGAAGGA
GGTGTGGAAAGTGAGGAGGAATCAGAATCAGGTAGTAGTAGCAGTAGTAGCGAAAGTCAGTCT
GGAGGTCCATGGGGCTATCAGGTACCAGCGTATGACAGAAGCAAGAATGCAAACCAAAAGAAG
TCGCCAGGAGCAAACTCTGAAGGTTACAACACAGCACTTTGA (SEQ ID NO: 93)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC5, EC6, EC9 and EC10 (V6) is set forth in SEQ ID NO: 94 (mini-PCDH15 V6: includes EC1-EC2-EC3-EC4--EC7-EC8-EC11-MAD12-TM-cyto CD3):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG
ATGGATGCAAATGATAACGCTCCAGTGTTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTG
GAAGAAGAAGCCAATGCCTTTGTGGGTCAAGTAAAAGCAACAGACCCTGATGCTGGAATAAAT
GGTCAAGTGCACTACAGTTTGGGTAACTTTAATAATCTTTTTCGTATCACATCCAATGGGAGC
ATTTACACAGCAGTGAAGCTTAACAGAGAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCA
ACAGATGGAGCAGTACACCCTCGTCATTCAACTCTAACCTTGGCCATCAAGGTTTTGGACATT
GATGATAACAGTCCTGTGTTCACCAATTCAACATACACTGTCCTTGTTGAAGAGAATTTGCCA
GCTGGGACTACCATCCTTCAAATAGAGGCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTAC
CGGATAAGAAGCCCAGAAGTGAAGCACTTTTTTGCACTACATCCATTTACAGGAGAACTATCG
CTTTTAAGGAGTTTAGATTATGAGGCATTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTA
GAGGCCTTTGATATTTATGGAACAATGCCACCTGGTATTGCTACTGTCACAGTGATTGTAAAG
GATATGAATGATTATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGAT
GCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGT
GTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAA
ACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAG
TTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTC
TCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAA
AAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCC
AAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTAC
ACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAAT
GAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTAT
GGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGA
GGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGC
TGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAG

TGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCT
GCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAA
CTTGGAGACAGCTCAATGCATAAGTATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTA
CCACCAGCTGGACAGGAGGAATATGGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAG
GAAGAGTGGGCAAGAAAAAGAATGATCAAGTTAGTTGTTGATCGAGAGTATGAAACCAGCTCA
ACTGGAGAAGACAGTGCTCCTGAATGTCAGAGAAACCGTCTTCACCATCCTAGTATCCACAGT
AATATCAACGGCAATATATATATTGCACAGAATGGTTCTGTGGTGAGAACCCGCCGTGCCTGC
CTCACGGACAACTTAAAAGTTGCTTCCCCTGTTCGACTGGGAGGGCCCTTTAAGAAACTAGAC
AAGTTGGCAGTGACACATGAGGAGAATGTACCTCTGAACACATTATCAAAGGGGCCATTTTCT
ACTGAAAAAATGAATGCAAGACCAACTCTGGTTACATTTGCCCCTTGCCCTGTGGGGACTGAC
AATACAGCGGTGAAGCCACTAAGGAACAGGCTGAAAAGCACAGTTGAACAGGAGTCCATGATT
GACAGTAAGAACATCAAGGAGGCTTTGGAATTTCATAGTGACCACACACAGTCTGATGATGAA
GAGCTTTGGATGGGCCCCTGGAACAACCTCCATATACCAATGACAAAACTGTGA (SEQ ID NO: 94)

In some embodiments, the mini-PCDH15 has 5 EC domains less than the full-length PCDH15. In some examples, the mini-PCDH15 lacks EC4, EC5, EC6, EC7 and EC8 domain. In some embodiments, the mini-PCDH15 includes EC1-EC2-EC3-EC9-EC10-EC11of SEQ ID NO: 1, 53, 55, or 57. In one example, the mini-PCDH15 comprises an amino acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 41, 95, or 96. In some embodiments, the nucleic acid encoding the mini-PCDH15 lacking EC4, EC5, EC6, EC7 and EC8 is at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 42, 97, or 98.

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC5, EC6, EC7 and EC8 (V4) is set forth in SEQ ID NO: 41 (mini-PCDH15 V4: includes EC1-EC2-EC3-EC9-EC10-EC11-MAD12-TM-cyto CD1; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQPPVFSKRIYKGMVAPDAVKGTPITTVYAEDADPPGLPASRVRYRV
DDVQFPYPASIFEVEEDSGRVITRVNLNEEPTTIFKLVVVAFDDGEPVMSSSATVKILVLHPG
E**IPRFTQEEYRPPPVSELATKGTMVGVISAAAINQSIVYSIVSGNEEDTFGINNITGVIYVNG**
PLDYETRTSYVLRVQADSLEVVLANLRVPSKSNTAKVYIEIQDENNHPPVFQKKFYIGGVSED
ARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFK
FQVIATDDYGKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGA
KVVVESIGARRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYY
GEGGRILEIRTPEAVTSIKKRGESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAE**
CTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELGDSSMHNLFLLYHFQQSRGN

NSVSEDRKHQQVVMPFSSNTIEAHKSAHVDGSLKSNKLKSARKFTFLSDEDDLSAHNPLYKEN
ISQVSTNSDISQRTDFVDPFSPKIQAKSKSLRGPREKIQRLWSQSVSLPRRLMRKVPNRPEII
DLQQWQGTRQKAENENTGICTNKRGSSNPLLTTEEANLTEKEEIRQGETLMIEGTEQLKSLSS
DSSFCFPRPHFSFSTLPTVSRTVELKSEPNVISSPAECSLELSPSRPCVLHSSLSRRETPICM
LPIETERNIFENFAHPPNISPSACPLPPPPPISPPSPPPAPAPLAPPPDISPFSLFCPPPSPP
SIPLPLPPPTFFPLSVSTSGPPTPPLLPPFPTPLPPPPPSIPCPPPPSASFLSTECVCITGVK
CTTNLMPAEKIKSSMTQLSTTTVCKTDPQREPKGILRHVKNLAELEKSVANMYSQIEKNYLRT
NVSELQTMCPSEVTNMEITSEQNKGSLNNIVEGTEKQSHSQSTSL (SEQ ID NO: 41)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC5, EC6, EC7 and EC8 (V4) is set forth in SEQ ID NO: 95 (mini-PCDH15 V4: includes EC1-EC2-EC3-EC9-EC10-EC11-MAD12-TM-cyto CD2; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEIL<u>**DENNQ**</u>PPVFSKRIYKGMVAPDAVKGTPITTVYAEDADPPGLPASRVRYRV
DDVQFPYPASIFEVEEDSGRVITRVNLNEEPTTIFKLVVVAFDDGEPVMSSSATVKILVLHPG
E**IPRFTQEEYRPPPVSELATKGTMVGVISAAAINQSIVYSIVSGNEEDTFGINNITGVIYVNG**
PLDYETRTSYVLRVQADSLEVVLANLRVPSKSNTAKVYIEIQDENNHPPVFQKKFYIGGVSED
ARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFK
FQVIATDDYGKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGA
KVVVESIGARRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYY
GEGGRILEIRTPEAVTSIKKRGESLGYTE**GALLAFLAFIIILCCIPAILVVLVSYRQFKVRQA**
ECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRL
LPPAGQEEYGEVVGEAEEEYEEEEEEPKKIKKPKVEIREPSEEEEVVVTIEKPPAAEPTYTTW
KRARIFPMIFKKVRGLADKRGIVDLEGEEWQRRLEEEDKDYLKLTLDQEEATESTVESEEESS
SDYTEYSEEESEFSESETTEEESESETPSEEEESSTPESEESESTESEGEKARKNIVLARRRP
MVEEVKEVKGRKEEPQEEQKEPKMEEEEHSEEEESGPAPVEESTDPEAQDIPEEGSAESASVE
GGVESEEESESGSSSSSSESQSGGPWGYQVPAYDRSKNANQKKSPGANSEGYNTAL (SEQ ID NO: 95)

An exemplary amino acid sequence of a miniPCDH15 lacking EC4, EC5, EC6, EC7 and EC8 (V4) is set forth in SEQ ID NO: 96 (mini-PCDH15 V4: includes EC1-EC2-EC3-EC9-EC10-EC11-MAD12-TM-cyto CD3; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH

PLPAFAGLHIEILDENNQPPVFSKRIYKGMVAPDAVKGTPITTVYAEDADPPGLPASRVRYRV
DDVQFPYPASIFEVEEDSGRVITRVNLNEEPTTIFKLVVVAFDDGEPVMSSSATVKILVLHPG
E**IPRFTQEEYRPPPVSELATKGTMVGVISAAAINQSIVYSIVSGNEEDTFGINNITGVIYVNG**
PLDYETRTSYVLRVQADSLEVVLANLRVPSKSNTAKVYIEIQDENNHPPVFQKKFYIGGVSED
ARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFK
FQVIATDDYGKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGA
KVVVESIGARRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYY
GEGGRILEIRTPEAVTSIKKRGESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAE**
CTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLL
PPAGQEEYGEVVGEAEEEYEEEEWARKRMIKLVVDREYETSSTGEDSAPECQRNRLHHPSIHS
NINGNIYIAQNGSVVRTRRACLTDNLKVASPVRLGGPFKKLDKLAVTHEENVPLNTLSKGPFS
TEKMNARPTLVTFAPCPVGTDNTAVKPLRNRLKSTVEQESMIDSKNIKEALEFHSDHTQSDDE
ELWMGPWNNLHIPMTKL (SEQ ID NO: 96)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC5, EC6, EC7 and EC8 (V4) is set forth in SEQ ID NO: 42 (mini-PCDH15 V4: includes EC1-EC2-EC3-EC9-EC10-EC11-MAD12-TM-cytoCD1):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAACCTCCTGTC
TTTAGTAAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTCAAGGGTACACCTATCACA
ACAGTTTATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGTCGTGTGAGGTATAGAGTA
GATGATGTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAAGAAGATTCTGGAAGAGTA
ATAACACGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAGTTGGTGGTGGTTGCTTTT
GATGATGGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATTCTTGTCTTACATCCTGGT
GAGATCCCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTAAGTGAACTTGCCACCAAA
GGGACCATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGTATTGTGTACTCCATTGTT
TCAGGAAATGAAGAAGATACATTTGGAATTAATAACATCACAGGTGTTATCTATGTGAATGGA
CCTCTGGATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAAGCTGATTCCCTGGAAGTG
GTCCTTGCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAAGTATACATTGAGATTCAG

GATGAAAATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGAT
GCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGT
GTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAA
ACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAG
TTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTC
TCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAA
AAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCC
AAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTAC
ACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAAT
GAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTAT
GGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGA
GGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGC
TGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAG
TGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCT
GCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAA
CTTGGAGACAGCTCAATGCATAATCTTTTCCTTCTCTACCATTTTCAACAAAGCAGGGGAAAT
AACTCAGTCTCAGAAGACAGGAAACATCAACAAGTTGTGATGCCCTTTTCTTCCAATACTATT
GAGGCTCACAAGTCAGCTCATGTAGACGGATCACTTAAGAGCAACAAACTGAAGTCTGCAAGA
AAATTCACATTTCTATCTGATGAGGATGACTTAAGTGCCCATAATCCCCTTTATAAGGAAAAC
ATAAGTCAAGTATCAACAAATTCAGACATTTCACAGAGAACAGATTTTGTAGACCCATTTTCA
CCCAAAATACAAGCCAAGAGTAAGTCTCTGAGGGGCCCAAGAGAAAAGATTCAGAGGCTGTGG
AGTCAGTCAGTCAGCTTACCCAGGAGGCTGATGAGGAAAGTTCCAAATAGACCAGAGATCATA
GATCTGCAGCAGTGGCAAGGCACCAGGCAGAAAGCTGAAAATGAAAACACTGGAATCTGTACA
AACAAAAGAGGTAGCAGCAATCCATTGCTTACAACTGAAGAGGCAAATTTGACAGAGAAAGAG
GAAATAAGGCAAGGTGAAACACTGATGATAGAAGGAACAGAACAGTTGAAATCTCTCTCTTCA
GACTCTTCATTTTGCTTTCCCAGGCCTCACTTCTCATTCTCCACTTTGCCAACTGTTTCAAGA
ACTGTGGAACTCAAATCAGAACCTAATGTCATCAGTTCTCCTGCTGAGTGTTCCTTGGAACTT
TCTCCTTCAAGGCCTTGTGTTTTACATTCTTCACTCTCTAGGAGAGAGACACCTATTTGTATG
TTACCTATTGAAACCGAAAGAAATATTTTTGAAAATTTTGCCCATCCACCAAACATCTCTCCT
TCTGCCTGTCCCCTTCCCCCTCCTCCTCCTATTTCTCCTCCTTCTCCTCCTCCTGCTCCTGCT
CCTCTTGCTCCTCCTCCTGACATTTCTCCTTTTTTCTCTTTTTTTGTCCTCCTCCCTCTCCTCCT
TCTATCCCTCTTCCTCTTCCTCCTCCTACATTTTTTCCACTTTCCGTTTCAACGTCTGGTCCC
CCAACACCACCTCTTCTACCTCCATTTCCAACTCCTCTTCCTCCACCACCTCCTTCTATTCCT
TGCCCTCCACCTCCTTCAGCTTCATTTCTGTCCACAGAGTGTGTCTGTATAACAGGTGTTAAA
TGCACGACCAACTTGATGCCTGCCGAGAAAATTAAGTCCTCTATGACACAGCTATCAACAACG
ACAGTGTGTAAAACAGACCCTCAGAGAGAACCAAAAGGCATCCTCAGACACGTTAAAAACTTA
GCAGAACTTGAAAAATCAGTAGCTAACATGTACAGTCAAATAGAAAAAAACTATCTACGCACA
AATGTTTCAGAACTTCAAACTATGTGCCCTTCAGAAGTAACAAATATGGAAATCACATCTGAA
CAAAACAAGGGGAGTTTGAACAATATTGTCGAGGGAACTGAAAAACAATCTCACAGTCAATCT
ACTTCACTGTAA (SEQ ID NO: 42)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC5, EC6, EC7 and EC8 (V4) is set forth in SEQ ID NO: 97 (mini-PCDH15 V4: includes EC1-EC2-EC3-EC9-EC10-EC11-MAD12-TM-cytoCD2):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA

GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAACCTCCTGTC
TTTAGTAAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTCAAGGGTACACCTATCACA
ACAGTTTATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGTCGTGTGAGGTATAGAGTA
GATGATGTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAAGAAGATTCTGGAAGAGTA
ATAACACGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAGTTGGTGGTGGTTGCTTTT
GATGATGGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATTCTTGTCTTACATCCTGGT
GAGATCCCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTAAGTGAACTTGCCACCAAA
GGGACCATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGTATTGTGTACTCCATTGTT
TCAGGAAATGAAGAAGATACATTTGGAATTAATAACATCACAGGTGTTATCTATGTGAATGGA
CCTCTGGATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAAGCTGATTCCCTGGAAGTG
GTCCTTGCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAAGTATACATTGAGATTCAG
GATGAAAATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGAT
GCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGT
GTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAA
ACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAG
TTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTC
TCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAA
AAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCC
AAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTAC
ACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAAT
GAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTAT
GGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGA
GGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGC
TGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAG
TGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCT
GCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAA
CTTGGAGACAGCTCAATGCATAAGTATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTA
CCACCAGCTGGACAGGAGGAATATGGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAG
GAAGAGGAAGAGCCAAAGAAAATTAAAAAACCAAAGGTTGAAATTAGAGAGCCTAGTGAGGAG
GAAGAAGTAGTTGTAACTATCGAAAAACCACCAGCAGCTGAGCCTACATACACAACATGGAAG
AGAGCCAGAATATTCCCCATGATTTTTAAGAAAGTTAGAGGATTAGCTGATAAAAGAGGAATC

GTTGACCTTGAGGGTGAAGAGTGGCAGAGACGCCTTGAGGAAGAAGATAAAGATTATTTGAAA
CTCACTCTGGACCAAGAGGAAGCAACAGAAAGCACTGTAGAATCAGAGGAGGAATCCTCCAGC
GACTATACTGAATACAGTGAAGAAGAGTCTGAGTTCAGTGAGTCTGAGACTACAGAAGAGGAA
TCTGAGTCAGAGACACCCTCTGAGGAGGAGGAGAGTTCCACCCCTGAATCAGAAGAATCGGAA
TCCACAGAGTCAGAAGGAGAAAAAGCAAGGAAAAACATTGTGCTTGCAAGAAGAAGGCCCATG
GTTGAGGAGGTCAAGGAAGTCAAGGGTAGGAAAGAGGAGCCACAAGAAGAACAAAAAGAACCT
AAGATGGAAGAAGAAGAACACTCAGAAGAAGAAGAAAGTGGACCAGCCCCTGTGGAAGAAAGT
ACAGACCCTGAAGCTCAAGATATCCCTGAAGAGGGCAGTGCAGAATCAGCTTCGGTGGAAGGA
GGTGTGGAAAGTGAGGAGGAATCAGAATCAGGTAGTAGTAGCAGTAGTAGCGAAAGTCAGTCT
GGAGGTCCATGGGGCTATCAGGTACCAGCGTATGACAGAAGCAAGAATGCAAACCAAAAGAAG
TCGCCAGGAGCAAACTCTGAAGGTTACAACACAGCACTTTGA (SEQ ID NO: 97)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC5, EC6, EC7 and EC8 (V4) is set forth in SEQ ID NO: 98 (mini-PCDH15 V4: includes EC1-EC2-EC3-EC9-EC10-EC11-MAD12-TM-cytoCD3):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAACCTCCTGTC
TTTAGTAAACGAATATACAAAGGGATGGTGGCTCCGGATGCAGTCAAGGGTACACCTATCACA
ACAGTTTATGCTGAAGATGCAGACCCTCCTGGATTACCTGCAAGTCGTGTGAGGTATAGAGTA
GATGATGTACAGTTTCCTTACCCTGCCAGTATTTTTGAAGTGGAAGAAGATTCTGGAAGAGTA
ATAACACGAGTCAATCTTAATGAAGAACCTACAACAATTTTTAAGTTGGTGGTGGTTGCTTTT
GATGATGGGGAGCCTGTGATGTCCAGCAGTGCCACAGTGAAGATTCTTGTCTTACATCCTGGT
GAGATCCCACGCTTCACACAGGAGGAATATAGACCTCCTCCAGTAAGTGAACTTGCCACCAAA
GGGACCATGGTTGGTGTAATTTCTGCTGCTGCCATTAATCAAAGTATTGTGTACTCCATTGTT
TCAGGAAATGAAGAAGATACATTTGGAATTAATAACATCACAGGTGTTATCTATGTGAATGGA
CCTCTGGATTATGAGACCAGGACAAGCTATGTACTTCGAGTCCAAGCTGATTCCCTGGAAGTG
GTCCTTGCCAATCTCCGAGTTCCTTCAAAAAGCAATACAGCTAAAGTATACATTGAGATTCAG
GATGAAAATAATCATCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGAT
GCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGT

GTCATGGCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAA
ACATATACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAG
TTTCAAGTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTC
TCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAA
AAAAAGATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCC
AAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTAC
ACCAAATGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAAT
GAGCTTTTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTAT
GGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGA
GGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGC
TGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAG
TGTACAAAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCT
GCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAA
CTTGGAGACAGCTCAATGCATAAGTATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTA
CCACCAGCTGGACAGGAGGAATATGGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAG
GAAGAGTGGGCAAGAAAAAGAATGATCAAGTTAGTTGTTGATCGAGAGTATGAAACCAGCTCA
ACTGGAGAAGACAGTGCTCCTGAATGTCAGAGAAACCGTCTTCACCATCCTAGTATCCACAGT
AATATCAACGGCAATATATATATTGCACAGAATGGTTCTGTGGTGAGAACCCGCCGTGCCTGC
CTCACGGACAACTTAAAAGTTGCTTCCCCTGTTCGACTGGGAGGGCCCTTTAAGAAACTAGAC
AAGTTGGCAGTGACACATGAGGAGAATGTACCTCTGAACACATTATCAAAGGGGCCATTTTCT
ACTGAAAAAATGAATGCAAGACCAACTCTGGTTACATTTGCCCCTTGCCCTGTGGGGACTGAC
AATACAGCGGTGAAGCCACTAAGGAACAGGCTGAAAAGCACAGTTGAACAGGAGTCCATGATT
GACAGTAAGAACATCAAGGAGGCTTTGGAATTTCATAGTGACCACACACAGTCTGATGATGAA
GAGCTTTGGATGGGCCCCTGGAACAACCTCCATATACCAATGACAAAACTGTGA (SEQ ID NO: 98)

In some examples, the mini-PCDH15 lacks EC4, EC5, EC6, EC9 and EC10 domain. In some embodiments, the mini-PCDH15 includes EC1-EC2-EC3-EC7-EC8-EC11of SEQ ID NO: 1, 53, 55, or 57. In one example, the mini-PCDH15 comprises an amino acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 43, 99 or 100. In some embodiments, the nucleic acid encoding the mini-PCDH15 lacking EC4, EC5, EC6, EC9 and EC10 is at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 44, 101 or 102.

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC5, EC6, EC9 and EC10 (V7) is set forth in SEQ ID NO: 43 (mini-PCDH15 V7: includes EC1-EC2-EC3-EC7-EC8-EC11-MAD12-TM-cyto CD1; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN

GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQAPVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQVHYSLGN
FNNLFRITSNGSIYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDDN**SPVFTN**
STYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTGELSLLRSLDYEA
FPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDYPPVFQKKFYIGGVSEDARMFTSVLR
VKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDY
GKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGA
RRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEI
RTPEAVTSIKKRGESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQA**
ALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELGDSSMHNLFLLYHFQQSRGNNSVSEDRKH
QQVVMPFSSNTIEAHKSAHVDGSLKSNKLKSARKFTFLSDEDDLSAHNPLYKENISQVSTNSD
ISQRTDFVDPFSPKIQAKSKSLRGPREKIQRLWSQSVSLPRRLMRKVPNRPEIIDLQQWQGTR
QKAENENTGICTNKRGSSNPLLTTEEANLTEKEEIRQGETLMIEGTEQLKSLSSDSSFCFPRP
HFSFSTLPTVSRTVELKSEPNVISSPAECSLELSPSRPCVLHSSLSRRETPICMLPIETERNI
FENFAHPPNISPSACPLPPPPPISPPSPPPAPAPLAPPPDISPFSLFCPPPSPPSIPLPLPPP
TFFPLSVSTSGPPTPPLLPPFPTPLPPPPPSIPCPPPPSASFLSTECVCITGVKCTTNLMPAE
KIKSSMTQLSTTTVCKTDPQREPKGILRHVKNLAELEKSVANMYSQIEKNYLRTNVSELQTMC
PSEVTNMEITSEQNKGSLNNIVEGTEKQSHSQSTSL (SEQ ID NO: 43)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC5, EC6, EC9 and EC10 (V7) is set forth in SEQ ID NO: 99 (mini-PCDH15 V7: includes EC1-EC2-EC3-EC7-EC8-EC11-MAD12-TM-cyto CD2; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQAPVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQVHYSLGN
FNNLFRITSNGSIYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDDN**SPVFTN**
STYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTGELSLLRSLDYEA
FPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDYPPVFQKKFYIGGVSEDARMFTSVLR
VKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDY
GKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGA
RRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEI
RTPEAVTSIKKRGESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQA**
ALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYG
EVVGEAEEEYEEEEEEPKKIKKPKVEIREPSEEEEVVVTIEKPPAAEPTYTTWKRARIFPMIF
KKVRGLADKRGIVDLEGEEWQRRLEEEDKDYLKLTLDQEEATESTVESEEESSSDYTEYSEEE
SEFSESETTEEESESETPSEEEESSTPESEESESTESEGEKARKNIVLARRRPMVEEVKEVKG

RKEEPQEEQKEPKMEEEEHSEEEESGPAPVEESTDPEAQDIPEEGSAESASVEGGVESEEESE SGSSSSSSESQSGGPWGYQVPAYDRSKNANQKKSPGANSEGYNTAL (SEQ ID NO: 99)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC5, EC6, EC9 and EC10 (V7) is set forth in SEQ ID NO: 100 (mini-PCDH15 V7: includes EC1-EC2-EC3-EC7-EC8-EC11-MAD12-TM-cyto CD3; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI NKKVGTIIYHEVRIVVRDRNDN**SPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH PLPAFAGLHIEILDENNQ**APVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQVHYSLGN FNNLFRITSNGSIYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDDN**SPVFTN STYTVLVEENLPAGTTILQIEAKDVDLGANVSYRIRSPEVKHFFALHPFTGELSLLRSLDYEA FPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDY**PPVFQKKFYIGGVSEDARMFTSVLR VKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDY GKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGA RRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEI RTPEAVTSIKKRGESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQA ALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYG EVVGEAEEEYEEEEWARKRMIKLVVDREYETSSTGEDSAPECQRNRLHHPSIHSNINGNIYIA QNGSVVRTRRACLTDNLKVASPVRLGGPFKKLDKLAVTHEENVPLNTLSKGPFSTEKMNARPT LVTFAPCPVGTDNTAVKPLRNRLKSTVEQESMIDSKNIKEALEFHSDHTQSDDEELWMGPWNN LHIPMTKL** (SEQ ID NO: 100)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC5, EC6, EC9 and EC10 (V7) is set forth in SEQ ID NO: 44 (mini-PCDH15 V7: includes EC1-EC2-EC3-EC7-EC8-EC11-MAD12-TM-cyto CD1):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC

ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAGCTCCAGTG
TTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTGGAAGAAGAAGCCAATGCCTTTGTGGGT
CAAGTAAAAGCAACAGACCCTGATGCTGGAATAAATGGTCAAGTGCACTACAGTTTGGGTAAC
TTTAATAATCTTTTTCGTATCACATCCAATGGGAGCATTTACACAGCAGTGAAGCTTAACAGA
GAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCAACAGATGGAGCAGTACACCCTCGTCAT
TCAACTCTAACCTTGGCCATCAAGGTTTTGGACATTGATGATAACAGTCCTGTGTTCACCAAT
TCAACATACACTGTCCTTGTTGAAGAGAATTTGCCAGCTGGGACTACCATCCTTCAAATAGAG
GCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTACCGGATAAGAAGCCCAGAAGTGAAGCAC
TTTTTTGCACTACATCCATTTACAGGAGAACTATCGCTTTTAAGGAGTTTAGATTATGAGGCA
TTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTAGAGGCCTTTGATATTTATGGAACAATG
CCACCTGGTATTGCTACTGTCACAGTGATTGTAAAGGATATGAATGATTATCCCCCAGTGTTT
CAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGA
GTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCA
CCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCT
ATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTAT
GGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAA
GTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATC
TTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCT
CGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCA
ATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAA
CTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATC
CGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGG
GCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTG
GTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCC
GCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCG
CCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAATCTT
TTCCTTCTCTACCATTTTCAACAAAGCAGGGGAAATAACTCAGTCTCAGAAGACAGGAAACAT
CAACAAGTTGTGATGCCCTTTTCTTCCAATACTATTGAGGCTCACAAGTCAGCTCATGTAGAC
GGATCACTTAAGAGCAACAAACTGAAGTCTGCAAGAAAATTCACATTTCTATCTGATGAGGAT
GACTTAAGTGCCCATAATCCCCTTTATAAGGAAAACATAAGTCAAGTATCAACAAATTCAGAC
ATTTCACAGAGAACAGATTTTGTAGACCCATTTTCACCCAAAATACAAGCCAAGAGTAAGTCT
CTGAGGGGCCCAAGAGAAAAGATTCAGAGGCTGTGGAGTCAGTCAGTCAGCTTACCCAGGAGG
CTGATGAGGAAAGTTCCAAATAGACCAGAGATCATAGATCTGCAGCAGTGGCAAGGCACCAGG
CAGAAAGCTGAAAATGAAAACACTGGAATCTGTACAAACAAAAGAGGTAGCAGCAATCCATTG
CTTACAACTGAAGAGGCAAATTTGACAGAGAAAGAGGAAATAAGGCAAGGTGAAACACTGATG
ATAGAAGGAACAGAACAGTTGAAATCTCTCTCTTCAGACTCTTCATTTTGCTTTCCCAGGCCT
CACTTCTCATTCTCCACTTTGCCAACTGTTTCAAGAACTGTGGAACTCAAATCAGAACCTAAT
GTCATCAGTTCTCCTGCTGAGTGTTCCTTGGAACTTTCTCCTTCAAGGCCTTGTGTTTTACAT
TCTTCACTCTCTAGGAGAGAGACACCTATTTGTATGTTACCTATTGAAACCGAAAGAAATATT
TTTGAAAATTTTGCCCATCCACCAAACATCTCTCCTTCTGCCTGTCCCCTTCCCCCTCCTCCT
CCTATTTCTCCTCCTTCTCCTCCTCCTGCTCCTGCTCCTCTTGCTCCTCCTCCTGACATTTCT

CCTTTTTCTCTTTTTTGTCCTCCTCCCTCTCCTCCTTCTATCCCTCTTCCTCTTCCTCCTCCT
ACATTTTTTCCACTTTCCGTTTCAACGTCTGGTCCCCCAACACCACCTCTTCTACCTCCATTT
CCAACTCCTCTTCCTCCACCACCTCCTTCTATTCCTTGCCCTCCACCTCCTTCAGCTTCATTT
CTGTCCACAGAGTGTGTCTGTATAACAGGTGTTAAATGCACGACCAACTTGATGCCTGCCGAG
AAAATTAAGTCCTCTATGACACAGCTATCAACAACGACAGTGTGTAAAACAGACCCTCAGAGA
GAACCAAAAGGCATCCTCAGACACGTTAAAAACTTAGCAGAACTTGAAAAATCAGTAGCTAAC
ATGTACAGTCAAATAGAAAAAAACTATCTACGCACAAATGTTTCAGAACTTCAAACTATGTGC
CCTTCAGAAGTAACAAATATGGAAATCACATCTGAACAAAACAAGGGGAGTTTGAACAATATT
GTCGAGGGAACTGAAAAACAATCTCACAGTCAATCTACTTCACTGTAA (SEQ ID NO: 44)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC5, EC6, EC9 and EC10 (V7) is set forth in SEQ ID NO: 101 (mini-PCDH15 V7: includes EC1-EC2-EC3-EC7-EC8-EC11-MAD12-TM-cyto CD2):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAGCTCCAGTG
TTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTGGAAGAAGAAGCCAATGCCTTTGTGGGT
CAAGTAAAAGCAACAGACCCTGATGCTGGAATAAATGGTCAAGTGCACTACAGTTTGGGTAAC
TTTAATAATCTTTTTCGTATCACATCCAATGGGAGCATTTACACAGCAGTGAAGCTTAACAGA
GAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCAACAGATGGAGCAGTACACCCTCGTCAT
TCAACTCTAACCTTGGCCATCAAGGTTTTGGACATTGATGATAACAGTCCTGTGTTCACCAAT
TCAACATACACTGTCCTTGTTGAAGAGAATTTGCCAGCTGGGACTACCATCCTTCAAATAGAG
GCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTACCGGATAAGAAGCCCAGAAGTGAAGCAC
TTTTTTGCACTACATCCATTTACAGGAGAACTATCGCTTTTAAGGAGTTTAGATTATGAGGCA
TTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTAGAGGCCTTTGATATTTATGGAACAATG
CCACCTGGTATTGCTACTGTCACAGTGATTGTAAAGGATATGAATGATTATCCCCCAGTGTTT
CAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGA
GTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCA
CCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCT
ATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTAT

GGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAA
GTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATC
TTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCT
CGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCA
ATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAA
CTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATC
CGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGG
GCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTG
GTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCC
GCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCG
CCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAGTAT
GAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATATGGT
GAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAGGAAGAGCCAAAGAAAATTAAA
AAACCAAAGGTTGAAATTAGAGAGCCTAGTGAGGAGGAAGAAGTAGTTGTAACTATCGAAAAA
CCACCAGCAGCTGAGCCTACATACACAACATGGAAGAGAGCCAGAATATTCCCCATGATTTTT
AAGAAAGTTAGAGGATTAGCTGATAAAAGAGGAATCGTTGACCTTGAGGGTGAAGAGTGGCAG
AGACGCCTTGAGGAAGAAGATAAAGATTATTTGAAACTCACTCTGGACCAAGAGGAAGCAACA
GAAAGCACTGTAGAATCAGAGGAGGAATCCTCCAGCGACTATACTGAATACAGTGAAGAAGAG
TCTGAGTTCAGTGAGTCTGAGACTACAGAAGAGGAATCTGAGTCAGAGACACCCTCTGAGGAG
GAGGAGAGTTCCACCCCTGAATCAGAAGAATCGGAATCCACAGAGTCAGAAGGAGAAAAAGCA
AGGAAAAACATTGTGCTTGCAAGAAGAAGGCCCATGGTTGAGGAGGTCAAGGAAGTCAAGGGT
AGGAAAGAGGAGCCACAAGAAGAACAAAAAGAACCTAAGATGGAAGAAGAAGAACACTCAGAA
GAAGAAGAAAGTGGACCAGCCCCTGTGGAAGAAAGTACAGACCCTGAAGCTCAAGATATCCCT
GAAGAGGGCAGTGCAGAATCAGCTTCGGTGGAAGGAGGTGTGGAAAGTGAGGAGGAATCAGAA
TCAGGTAGTAGTAGCAGTAGTAGCGAAAGTCAGTCTGGAGGTCCATGGGGCTATCAGGTACCA
GCGTATGACAGAAGCAAGAATGCAAACCAAAAGAAGTCGCCAGGAGCAAACTCTGAAGGTTAC
AACACAGCACTTTGA (SEQ ID NO: 101)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC4, EC5, EC6, EC9 and EC10 (V7) is set forth in SEQ ID NO: 102 (mini-PCDH15 V7: includes EC1-EC2-EC3-EC7-EC8-EC11-MAD12-TM-cyto CD3):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG

AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAGCTCCAGTG
TTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTGGAAGAAGAAGCCAATGCCTTTGTGGGT
CAAGTAAAAGCAACAGACCCTGATGCTGGAATAAATGGTCAAGTGCACTACAGTTTGGGTAAC
TTTAATAATCTTTTTCGTATCACATCCAATGGGAGCATTTACACAGCAGTGAAGCTTAACAGA
GAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCAACAGATGGAGCAGTACACCCTCGTCAT
TCAACTCTAACCTTGGCCATCAAGGTTTTGGACATTGATGATAACAGTCCTGTGTTCACCAAT
TCAACATACACTGTCCTTGTTGAAGAGAATTTGCCAGCTGGGACTACCATCCTTCAAATAGAG
GCCAAAGATGTCGACCTTGGAGCAAATGTGTCTTACCGGATAAGAAGCCCAGAAGTGAAGCAC
TTTTTTGCACTACATCCATTTACAGGAGAACTATCGCTTTTAAGGAGTTTAGATTATGAGGCA
TTTCCAGACCAAGAAGCAAGTATCACTTTTCTGGTAGAGGCCTTTGATATTTATGGAACAATG
CCACCTGGTATTGCTACTGTCACAGTGATTGTAAAGGATATGAATGATTATCCCCCAGTGTTT
CAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGA
GTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCA
CCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCT
ATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTAT
GGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAA
GTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATC
TTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCT
CGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCA
ATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAA
CTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATC
CGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGG
GCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTG
GTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCC
GCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCG
CCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAGTAT
GAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATATGGT
GAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAGTGGGCAAGAAAAAGAATGATC
AAGTTAGTTGTTGATCGAGAGTATGAAACCAGCTCAACTGGAGAAGACAGTGCTCCTGAATGT
CAGAGAAACCGTCTTCACCATCCTAGTATCCACAGTAATATCAACGGCAATATATATATTGCA
CAGAATGGTTCTGTGGTGAGAACCCGCCGTGCCTGCCTCACGGACAACTTAAAAGTTGCTTCC
CCTGTTCGACTGGGAGGGCCCTTTAAGAAACTAGACAAGTTGGCAGTGACACATGAGGAGAAT
GTACCTCTGAACACATTATCAAAGGGGCCATTTTCTACTGAAAAAATGAATGCAAGACCAACT
CTGGTTACATTTGCCCCTTGCCCTGTGGGGACTGACAATACAGCGGTGAAGCCACTAAGGAAC
AGGCTGAAAAGCACAGTTGAACAGGAGTCCATGATTGACAGTAAGAACATCAAGGAGGCTTTG
GAATTTCATAGTGACCACACACAGTCTGATGATGAAGAGCTTTGGATGGGCCCCTGGAACAAC
CTCCATATACCAATGACAAAACTGTGA (SEQ ID NO: 102)

In some examples, the mini-PCDH15 lacks EC5, EC6, EC8, EC9 and EC10 domain. In some embodiments, the mini-PCDH15 includes EC1-EC2-EC3-EC4-EC7-EC11 of SEQ ID NO: 1, 53, 55, or 57. In one example, the mini-PCDH15 comprises an amino acid sequence at

least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 45, 103, or 104. In some embodiments, the nucleic acid encoding the mini-PCDH15 lacking EC5, EC6, EC8, EC9 and EC10 is at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 46, 105, or 106.

An exemplary amino acid sequence of a mini-PCDH15 lacking EC5, EC6, EC8, EC9 and EC10 (V8) is set forth in SEQ ID NO: 45 (mini-PCDH15 V8: includes EC1-EC2-EC3-EC4-EC7-EC11-MAD12-TM-cyto CD1; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT
KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV
MDANDN**APVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQVHYSLGNFNNLFRITSNGS**
IYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDDNPPVFQKKFYIGGVSEDAR
MFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQ
VIATDDYGKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKV
VVESIGARRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGE
GGRILEIRTPEAVTSIKKRGESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECT**
KTARIQAALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELGDSSMHNLFLLYHFQQSRGNNS
VSEDRKHQQVVMPFSSNTIEAHKSAHVDGSLKSNKLKSARKFTFLSDEDDLSAHNPLYKENIS
QVSTNSDISQRTDFVDPFSPKIQAKSKSLRGPREKIQRLWSQSVSLPRRLMRKVPNRPEIIDL
QQWQGTRQKAENENTGICTNKRGSSNPLLTTEEANLTEKEEIRQGETLMIEGTEQLKSLSSDS
SFCFPRPHFSFSTLPTVSRTVELKSEPNVISSPAECSLELSPSRPCVLHSSLSRRETPICMLP
IETERNIFENFAHPPNISPSACPLPPPPPISPPSPPPAPAPLAPPPDISPFSLFCPPPSPPSI
PLPLPPPTFFPLSVSTSGPPTPPLLPPFPTPLPPPPPSIPCPPPPSASFLSTECVCITGVKCT
TNLMPAEKIKSSMTQLSTTTVCKTDPQREPKGILRHVKNLAELEKSVANMYSQIEKNYLRTNV
SELQTMCPSEVTNMEITSEQNKGSLNNIVEGTEKQSHSQSTSL (SEQ ID NO: 45)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC5, EC6, EC8, EC9 and EC10 (V8) is set forth in SEQ ID NO: 103 (mini-PCDH15 V8: includes EC1-EC2-EC3-EC4-EC7-EC11-MAD12-TM-cyto CD2; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN

GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT
KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV
MDANDN**APVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQVHYSLGNFNNLFRITSNGS**
IYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDDNPPVFQKKFYIGGVSEDAR
MFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQ
VIATDDYGKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKV
VVESIGARRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGE
GGRILEIRTPEAVTSIKKRGESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECT**
KTARIQAALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPP
AGQEEYGEVVGEAEEEYEEEEEEPKKIKKPKVEIREPSEEEEVVVTIEKPPAAEPTYTTWKRA
RIFPMIFKKVRGLADKRGIVDLEGEEWQRRLEEEDKDYLKLTLDQEEATESTVESEEESSSDY
TEYSEEESEFSESETTEEESESETPSEEEESSTPESEESESTESEGEKARKNIVLARRRPMVE
EVKEVKGRKEEPQEEQKEPKMEEEEHSEEEESGPAPVEESTDPEAQDIPEEGSAESASVEGGV
ESEEESESGSSSSSSESQSGGPWGYQVPAYDRSKNANQKKSPGANSEGYNTAL (SEQ ID NO: 103)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC5, EC6, EC8, EC9 and EC10 (V8) is set forth in SEQ ID NO: 104 (mini-PCDH15 V8: includes EC1-EC2-EC3-EC4-EC7-EC11-MAD12-TM-cyto CD3; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQSPYFTMPSYQGYILESAPVGATISDSLNLTSPLRIVALDKDIEDT
KDPELHLFLNDYTSVFTVTQTGITRYLTLLQPVDREEQQTYTFSITAFDGVQESEPVIVNIQV
MDANDN**APVFDPYLPRNLSVVEEEANAFVGQVKATDPDAGINGQVHYSLGNFNNLFRITSNGS**
IYTAVKLNREVRDYYELVVVATDGAVHPRHSTLTLAIKVLDIDDNPPVFQKKFYIGGVSEDAR
MFTSVLRVKATDKDTGNYSVMAYRLIIPPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQ
VIATDDYGKGLSGKADVLVSVVNQLDMQVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKV
VVESIGARRHGDAFSLEDYTKCDLTVYAIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGE
GGRILEIRTPEAVTSIKKRGESLGYTE**GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECT**
KTARIQAALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPP
AGQEEYGEVVGEAEEEYEEEEWARKRMIKLVVDREYETSSTGEDSAPECQRNRLHHPSIHSNI
NGNIYIAQNGSVVRTRRACLTDNLKVASPVRLGGPFKKLDKLAVTHEENVPLNTLSKGPFSTE
KMNARPTLVTFAPCPVGTDNTAVKPLRNRLKSTVEQESMIDSKNIKEALEFHSDHTQSDDEEL
WMGPWNNLHIPMTKL (SEQ ID NO: 104)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC5, EC6, EC8, EC9 and EC10 (V8) is set forth in SEQ ID NO: 46 (mini-PCDH15 V8: includes EC1-EC2-EC3-EC4-EC7-EC11-MAD12-TM-cyto CD1):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG
ATGGATGCAAATGATAACGCTCCAGTGTTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTG
GAAGAAGAAGCCAATGCCTTTGTGGGTCAAGTAAAAGCAACAGACCCTGATGCTGGAATAAAT
GGTCAAGTGCACTACAGTTTGGGTAACTTTAATAATCTTTTTCGTATCACATCCAATGGGAGC
ATTTACACAGCAGTGAAGCTTAACAGAGAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCA
ACAGATGGAGCAGTACACCCTCGTCATTCAACTCTAACCTTGGCCATCAAGGTTTTGGACATT
GATGATAACCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGA
ATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATG
GCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATAT
ACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAA
GTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTG
GTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAG
ATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTC
GTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAA
TGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTT
TTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAA
GGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAA
AGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATT
CCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACA
AAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCA

GTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGA
GACAGCTCAATGCATAATCTTTTCCTTCTCTACCATTTTCAACAAAGCAGGGGAAATAACTCA
GTCTCAGAAGACAGGAAACATCAACAAGTTGTGATGCCCTTTTCTTCCAATACTATTGAGGCT
CACAAGTCAGCTCATGTAGACGGATCACTTAAGAGCAACAAACTGAAGTCTGCAAGAAAATTC
ACATTTCTATCTGATGAGGATGACTTAAGTGCCCATAATCCCCTTTATAAGGAAAACATAAGT
CAAGTATCAACAAATTCAGACATTTCACAGAGAACAGATTTTGTAGACCCATTTTCACCCAAA
ATACAAGCCAAGAGTAAGTCTCTGAGGGGCCCAAGAGAAAAGATTCAGAGGCTGTGGAGTCAG
TCAGTCAGCTTACCCAGGAGGCTGATGAGGAAAGTTCCAAATAGACCAGAGATCATAGATCTG
CAGCAGTGGCAAGGCACCAGGCAGAAAGCTGAAAATGAAAACACTGGAATCTGTACAAACAAA
AGAGGTAGCAGCAATCCATTGCTTACAACTGAAGAGGCAAATTTGACAGAGAAAGAGGAAATA
AGGCAAGGTGAAACACTGATGATAGAAGGAACAGAACAGTTGAAATCTCTCTCTTCAGACTCT
TCATTTTGCTTTCCCAGGCCTCACTTCTCATTCTCCACTTTGCCAACTGTTTCAAGAACTGTG
GAACTCAAATCAGAACCTAATGTCATCAGTTCTCCTGCTGAGTGTTCCTTGGAACTTTCTCCT
TCAAGGCCTTGTGTTTTACATTCTTCACTCTCTAGGAGAGAGACACCTATTTGTATGTTACCT
ATTGAAACCGAAAGAAATATTTTTGAAAATTTTGCCCATCCACCAAACATCTCTCCTTCTGCC
TGTCCCCTTCCCCCTCCTCCTCCTATTTCTCCTCCTTCTCCTCCTCCTGCTCCTGCTCCTCTT
GCTCCTCCTCCTGACATTTCTCCTTTTTCTCTTTTTTGTCCTCCTCCCTCTCCTCCTTCTATC
CCTCTTCCTCTTCCTCCTCCTACATTTTTTCCACTTTCCGTTTCAACGTCTGGTCCCCCAACA
CCACCTCTTCTACCTCCATTTCCAACTCCTCTTCCTCCACCACCTCCTTCTATTCCTTGCCCT
CCACCTCCTTCAGCTTCATTTCTGTCCACAGAGTGTGTCTGTATAACAGGTGTTAAATGCACG
ACCAACTTGATGCCTGCCGAGAAAATTAAGTCCTCTATGACACAGCTATCAACAACGACAGTG
TGTAAAACAGACCCTCAGAGAGAACCAAAAGGCATCCTCAGACACGTTAAAAACTTAGCAGAA
CTTGAAAAATCAGTAGCTAACATGTACAGTCAAATAGAAAAAAACTATCTACGCACAAATGTT
TCAGAACTTCAAACTATGTGCCCTTCAGAAGTAACAAATATGGAAATCACATCTGAACAAAAC
AAGGGGAGTTTGAACAATATTGTCGAGGGAACTGAAAAACAATCTCACAGTCAATCTACTTCA
CTGTAA (SEQ ID NO: 46)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC5, EC6, EC8, EC9 and EC10 (V8) is set forth in SEQ ID NO: 105 (mini-PCDH15 V8: includes EC1-EC2-EC3-EC4-EC7-EC11-MAD12-TM-cyto CD2):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT

GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG
ATGGATGCAAATGATAACGCTCCAGTGTTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTG
GAAGAAGAAGCCAATGCCTTTGTGGGTCAAGTAAAAGCAACAGACCCTGATGCTGGAATAAAT
GGTCAAGTGCACTACAGTTTGGGTAACTTTAATAATCTTTTTCGTATCACATCCAATGGGAGC
ATTTACACAGCAGTGAAGCTTAACAGAGAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCA
ACAGATGGAGCAGTACACCCTCGTCATTCAACTCTAACCTTGGCCATCAAGGTTTTGGACATT
GATGATAACCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGA
ATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATG
GCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATAT
ACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAA
GTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTG
GTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAG
ATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTC
GTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAA
TGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTT
TTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAA
GGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAA
AGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATT
CCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACA
AAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCA
GTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGA
GACAGCTCAATGCATAAGTATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCA
GCTGGACAGGAGGAATATGGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAG
GAAGAGCCAAAGAAAATTAAAAAACCAAAGGTTGAAATTAGAGAGCCTAGTGAGGAGGAAGAA
GTAGTTGTAACTATCGAAAAACCACCAGCAGCTGAGCCTACATACACAACATGGAAGAGAGCC
AGAATATTCCCCATGATTTTTAAGAAAGTTAGAGGATTAGCTGATAAAAGAGGAATCGTTGAC
CTTGAGGGTGAAGAGTGGCAGAGACGCCTTGAGGAAGAAGATAAAGATTATTTGAAACTCACT
CTGGACCAAGAGGAAGCAACAGAAAGCACTGTAGAATCAGAGGAGGAATCCTCCAGCGACTAT
ACTGAATACAGTGAAGAAGAGTCTGAGTTCAGTGAGTCTGAGACTACAGAAGAGGAATCTGAG
TCAGAGACACCCTCTGAGGAGGAGGAGAGTTCCACCCCTGAATCAGAAGAATCGGAATCCACA
GAGTCAGAAGGAGAAAAAGCAAGGAAAAACATTGTGCTTGCAAGAAGAAGGCCCATGGTTGAG
GAGGTCAAGGAAGTCAAGGGTAGGAAAGAGGAGCCACAAGAAGAACAAAAAGAACCTAAGATG
GAAGAAGAAGAACACTCAGAAGAAGAAGAAAGTGGACCAGCCCCTGTGGAAGAAAGTACAGAC
CCTGAAGCTCAAGATATCCCTGAAGAGGGCAGTGCAGAATCAGCTTCGGTGGAAGGAGGTGTG
GAAAGTGAGGAGGAATCAGAATCAGGTAGTAGTAGCAGTAGTAGCGAAAGTCAGTCTGGAGGT
CCATGGGGCTATCAGGTACCAGCGTATGACAGAAGCAAGAATGCAAACCAAAAGAAGTCGCCA
GGAGCAAACTCTGAAGGTTACAACACAGCACTTTGA (SEQ ID NO: 105)

An exemplary nucleic acid sequence encoding a mini-PCDH15 lacking EC5, EC6, EC8, EC9 and EC10 (V8) is set forth in SEQ ID NO: 106 (mini-PCDH15 V8: includes EC1-EC2-EC3-EC4-EC7-EC11-MAD12-TM-cyto CD3):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAAAGTCCATAT
TTTACAATGCCCAGTTATCAAGGCTATATCCTGGAATCTGCCCCAGTGGGAGCAACCATTTCG
GACAGTCTCAATTTGACTTCACCTTTAAGAATAGTAGCTCTGGACAAGGACATAGAAGATACA
AAAGACCCAGAGCTTCACCTTTTTCTGAATGACTACACCTCAGTCTTCACCGTCACACAGACT
GGTATTACTCGCTACCTCACCTTACTTCAACCAGTGGACAGGGAAGAACAGCAAACTTACACC
TTTTCGATAACAGCATTTGATGGTGTACAAGAAAGTGAGCCAGTCATCGTCAATATTCAAGTG
ATGGATGCAAATGATAACGCTCCAGTGTTTGATCCTTATCTGCCAAGAAATTTATCTGTGGTG
GAAGAAGAAGCCAATGCCTTTGTGGGTCAAGTAAAAGCAACAGACCCTGATGCTGGAATAAAT
GGTCAAGTGCACTACAGTTTGGGTAACTTTAATAATCTTTTTCGTATCACATCCAATGGGAGC
ATTTACACAGCAGTGAAGCTTAACAGAGAAGTCAGGGACTACTATGAACTTGTTGTTGTGGCA
ACAGATGGAGCAGTACACCCTCGTCATTCAACTCTAACCTTGGCCATCAAGGTTTTGGACATT
GATGATAACCCCCCAGTGTTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGA
ATGTTTACTTCTGTACTCAGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATG
GCCTACAGACTCATAATACCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATAT
ACAGGGCTTATCAAAACTGCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAA
GTTATTGCAACTGACGACTATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTG
GTCAATCAGCTGGATATGCAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAG
ATAGAAGATCTTACAGAGATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTC
GTAGTGGAGTCCATTGGAGCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAA
TGTGACTTGACTGTCTATGCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTT
TTTAAATTTTTGGATGGCAAACTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAA
GGAGGACGCATTCTGGAGATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAA
AGTCTAGGATACACAGAAGGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATT
CCTGCCATCTTGGTGGTTTTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACA
AAGACTGCACGAATTCAGGCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCA

GTGGCAGCGCCCCCGCCGCCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGA
GACAGCTCAATGCATAAGTATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCA
GCTGGACAGGAGGAATATGGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAG
TGGGCAAGAAAAAGAATGATCAAGTTAGTTGTTGATCGAGAGTATGAAACCAGCTCAACTGGA
GAAGACAGTGCTCCTGAATGTCAGAGAAACCGTCTTCACCATCCTAGTATCCACAGTAATATC
AACGGCAATATATATATTGCACAGAATGGTTCTGTGGTGAGAACCCGCCGTGCCTGCCTCACG
GACAACTTAAAAGTTGCTTCCCCTGTTCGACTGGGAGGGCCCTTTAAGAAACTAGACAAGTTG
GCAGTGACACATGAGGAGAATGTACCTCTGAACACATTATCAAAGGGGCCATTTTCTACTGAA
AAAATGAATGCAAGACCAACTCTGGTTACATTTGCCCCTTGCCCTGTGGGGACTGACAATACA
GCGGTGAAGCCACTAAGGAACAGGCTGAAAAGCACAGTTGAACAGGAGTCCATGATTGACAGT
AAGAACATCAAGGAGGCTTTGGAATTTCATAGTGACCACACACAGTCTGATGATGAAGAGCTT
TGGATGGGCCCCTGGAACAACCTCCATATACCAATGACAAAACTGTGA (SEQ ID NO: 106)

In some embodiments, the mini-PCDH15 has 7 EC domains less than the full-length PCDH15. In some examples, the mini-PCDH15 lacks EC4, EC5, EC6, EC7, EC8, EC9, and EC10 domain. In some embodiments, the mini-PCDH15 includes EC1-EC2-EC3-EC11of SEQ ID NO: 1, 53, 55, or 57. In one example, the mini-PCDH15 comprises an amino acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 71, 107 or 108. In some embodiments, the nucleic acid encoding the mini-PCDH15 lacking EC4, EC5, EC6, EC7, EC8, EC9, and EC10 is at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 72, 109, or 110.

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V9) is set forth in SEQ ID NO: 71 (mini-PCDH15 V9: includes EC1-EC2-EC3- EC11-MAD12-TM-cyto CD1; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQPPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLII
PPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLD**M**
QVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVY
AIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE
GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPP
PPPPPPGAHLYEELGDSSMHNLFLLYHFQQSRGNNSVSEDRKHQQVVMPFSSNTIEAHKSAHV
DGSLKSNKLKSARKFTFLSDEDDLSAHNPLYKENISQVSTNSDISQRTDFVDPFSPKIQAKSK
SLRGPREKIQRLWSQSVSLPRRLMRKVPNRPEIIDLQQWQGTRQKAENENTGICTNKRGSSNP

LLTTEEANLTEKEEIRQGETLMIEGTEQLKSLSSDSSFCFPRPHFSFSTLPTVSRTVELKSEP
NVISSPAECSLELSPSRPCVLHSSLSRRETPICMLPIETERNIFENFAHPPNISPSACPLPPP
PPISPPSPPPAPAPLAPPPDISPFSLFCPPPSPPSIPLPLPPPTFFPLSVSTSGPPTPPLLPP
FPTPLPPPPPSIPCPPPPSASFLSTECVCITGVKCTTNLMPAEKIKSSMTQLSTTTVCKTDPQ
REPKGILRHVKNLAELEKSVANMYSQIEKNYLRTNVSELQTMCPSEVTNMEITSEQNKGSLNN
IVEGTEKQSHSQSTSL (SEQ ID NO: 71)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V9) is set forth in SEQ ID NO: 107 (mini-PCDH15 V9: includes EC1-EC2-EC3- EC11-MAD12-TM-cyto CD2; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQPPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLII
PPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLD**M**
QVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVY
AIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE
GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPP
PPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEEEPKKI
KKPKVEIREPSEEEEVVVTIEKPPAAEPTYTTWKRARIFPMIFKKVRGLADKRGIVDLEGEEW
QRRLEEEDKDYLKLTLDQEEATESTVESEEESSSDYTEYSEEESEFSESETTEEESESETPSE
EEESSTPESEESESTESEGEKARKNIVLARRRPMVEEVKEVKGRKEEPQEEQKEPKMEEEEHS
EEEESGPAPVEESTDPEAQDIPEEGSAESASVEGGVESEEESESGSSSSSSESQSGGPWGYQV
PAYDRSKNANQKKSPGANSEGYNTAL (SEQ ID NO: 107)

An exemplary amino acid sequence of a mini-PCDH15 lacking EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V9) is set forth in SEQ ID NO: 108 (mini-PCDH15 V9: includes EC1-EC2-EC3- EC11-MAD12-TM-cyto CD3; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**GPMFLPCVLVPNTRDCRPLTYQAAIPELRTPEELNPIIVTPPIQAIDQD**
RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELSLLEPVNRDFHQKFDLVIKAEQDNGH
PLPAFAGLHIEILDENNQPPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLII
PPIKEGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLD**M**
QVIVSNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVY

AIDPQTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE
GALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPP
PPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEWARKRM
IKLVVDREYETSSTGEDSAPECQRNRLHHPSIHSNINGNIYIAQNGSVVRTRRACLTDNLKVA
SPVRLGGPFKKLDKLAVTHEENVPLNTLSKGPFSTEKMNARPTLVTFAPCPVGTDNTAVKPLR
NRLKSTVEQESMIDSKNIKEALEFHSDHTQSDDEELWMGPWNNLHIPMTKL (SEQ ID NO: 108)

An exemplary nucleic acid sequence encoding a miniPCDH15 lacking EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V9) is set forth in SEQ ID NO: 72 (mini-PCDH15 V9: includes EC1-EC2-EC3- EC11-MAD12-TM-cyto CD1):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAACCCCCAGTG
TTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTC
AGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATA
CCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACT
GCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGAC
TATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATG
CAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAG
ATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGA
GCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTAT
GCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGC
AAACTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAG
ATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAA
GGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTT
TTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAG
GCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCG
CCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAT

CTTTTCCTTCTCTACCATTTTCAACAAAGCAGGGGAAATAACTCAGTCTCAGAAGACAGGAAA
CATCAACAAGTTGTGATGCCCTTTTCTTCCAATACTATTGAGGCTCACAAGTCAGCTCATGTA
GACGGATCACTTAAGAGCAACAAACTGAAGTCTGCAAGAAAATTCACATTTCTATCTGATGAG
GATGACTTAAGTGCCCATAATCCCCTTTATAAGGAAAACATAAGTCAAGTATCAACAAATTCA
GACATTTCACAGAGAACAGATTTTGTAGACCCATTTTCACCCAAAATACAAGCCAAGAGTAAG
TCTCTGAGGGGCCCAAGAGAAAAGATTCAGAGGCTGTGGAGTCAGTCAGTCAGCTTACCCAGG
AGGCTGATGAGGAAAGTTCCAAATAGACCAGAGATCATAGATCTGCAGCAGTGGCAAGGCACC
AGGCAGAAAGCTGAAAATGAAAACACTGGAATCTGTACAAACAAAAGAGGTAGCAGCAATCCA
TTGCTTACAACTGAAGAGGCAAATTTGACAGAGAAAGAGGAAATAAGGCAAGGTGAAACACTG
ATGATAGAAGGAACAGAACAGTTGAAATCTCTCTCTTCAGACTCTTCATTTTGCTTTCCCAGG
CCTCACTTCTCATTCTCCACTTTGCCAACTGTTTCAAGAACTGTGGAACTCAAATCAGAACCT
AATGTCATCAGTTCTCCTGCTGAGTGTTCCTTGGAACTTTCTCCTTCAAGGCCTTGTGTTTTA
CATTCTTCACTCTCTAGGAGAGAGACACCTATTTGTATGTTACCTATTGAAACCGAAAGAAAT
ATTTTTGAAAATTTTGCCCATCCACCAAACATCTCTCCTTCTGCCTGTCCCCTTCCCCCTCCT
CCTCCTATTTCTCCTCCTTCTCCTCCTCCTGCTCCTGCTCCTCTTGCTCCTCCTCCTGACATT
TCTCCTTTTTCTCTTTTTTGTCCTCCTCCCTCTCCTCCTTCTATCCCTCTTCCTCTTCCTCCT
CCTACATTTTTTCCACTTTCCGTTTCAACGTCTGGTCCCCCAACACCACCTCTTCTACCTCCA
TTTCCAACTCCTCTTCCTCCACCACCTCCTTCTATTCCTTGCCCTCCACCTCCTTCAGCTTCA
TTTCTGTCCACAGAGTGTGTCTGTATAACAGGTGTTAAATGCACGACCAACTTGATGCCTGCC
GAGAAAATTAAGTCCTCTATGACACAGCTATCAACAACGACAGTGTGTAAAACAGACCCTCAG
AGAGAACCAAAAGGCATCCTCAGACACGTTAAAAACTTAGCAGAACTTGAAAAATCAGTAGCT
AACATGTACAGTCAAATAGAAAAAAACTATCTACGCACAAATGTTTCAGAACTTCAAACTATG
TGCCCTTCAGAAGTAACAAATATGGAAATCACATCTGAACAAAACAAGGGGAGTTTGAACAAT
ATTGTCGAGGGAACTGAAAAACAATCTCACAGTCAATCTACTTCACTGTAA (SEQ ID NO: 72)

An exemplary nucleic acid sequence encoding a miniPCDH15 lacking EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V9) is set forth in SEQ ID NO: 109 (mini-PCDH15 V9: includes EC1-EC2-EC3- EC11-MAD12-TM-cyto CD2):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT

GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAACCCCCAGTG
TTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTC
AGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATA
CCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACT
GCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGAC
TATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATG
CAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAG
ATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGA
GCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTAT
GCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGC
AAACTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAG
ATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAA
GGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTT
TTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAG
GCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCG
CCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAG
TATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATAT
GGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAGGAAGAGCCAAAGAAAATT
AAAAAACCAAAGGTTGAAATTAGAGAGCCTAGTGAGGAGGAAGAAGTAGTTGTAACTATCGAA
AAACCACCAGCAGCTGAGCCTACATACACAACATGGAAGAGAGCCAGAATATTCCCCATGATT
TTTAAGAAAGTTAGAGGATTAGCTGATAAAAGAGGAATCGTTGACCTTGAGGGTGAAGAGTGG
CAGAGACGCCTTGAGGAAGAAGATAAAGATTATTTGAAACTCACTCTGGACCAAGAGGAAGCA
ACAGAAAGCACTGTAGAATCAGAGGAGGAATCCTCCAGCGACTATACTGAATACAGTGAAGAA
GAGTCTGAGTTCAGTGAGTCTGAGACTACAGAAGAGGAATCTGAGTCAGAGACACCCTCTGAG
GAGGAGGAGAGTTCCACCCCTGAATCAGAAGAATCGGAATCCACAGAGTCAGAAGGAGAAAAA
GCAAGGAAAAACATTGTGCTTGCAAGAAGAAGGCCCATGGTTGAGGAGGTCAAGGAAGTCAAG
GGTAGGAAAGAGGAGCCACAAGAAGAACAAAAAGAACCTAAGATGGAAGAAGAAGAACACTCA
GAAGAAGAAGAAAGTGGACCAGCCCCTGTGGAAGAAAGTACAGACCCTGAAGCTCAAGATATC
CCTGAAGAGGGCAGTGCAGAATCAGCTTCGGTGGAAGGAGGTGTGGAAAGTGAGGAGGAATCA
GAATCAGGTAGTAGTAGCAGTAGTAGCGAAAGTCAGTCTGGAGGTCCATGGGGCTATCAGGTA
CCAGCGTATGACAGAAGCAAGAATGCAAACCAAAAGAAGTCGCCAGGAGCAAACTCTGAAGGT
TACAACACAGCACTTTGA (SEQ ID NO: 109)

An exemplary nucleic acid sequence encoding a miniPCDH15 lacking EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V9) is set forth in SEQ ID NO: 110 (mini-PCDH15 V9: includes EC1-EC2-EC3- EC11-MAD12-TM-cyto CD3):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC

AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGGGTCCAATGTTTCTTCCTTGT
GTCCTTGTGCCAAACACTCGTGATTGCCGTCCACTCACTTATCAAGCTGCCATACCTGAGTTG
AGAACTCCGGAAGAACTGAACCCCATTATTGTTACGCCACCAATCCAAGCCATTGATCAGGAC
CGGAATATTCAACCGCCATCAGATAGGCCAGGAATCCTCTATTCCATCCTTGTTGGGACTCCT
GAGGATTACCCACGATTTTTCCATATGCATCCTAGGACAGCAGAACTTAGTCTCCTGGAGCCA
GTAAACAGAGACTTTCACCAGAAATTTGATTTGGTTATTAAGGCTGAACAAGACAATGGTCAT
CCTCTTCCTGCCTTTGCCGGTCTACACATTGAAATACTGGATGAAAACAATCAACCCCCAGTG
TTTCAGAAAAAATTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTC
AGAGTGAAGGCTACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATA
CCACCAATTAAAGAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACT
GCTATGCTCTTCCATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGAC
TATGGGAAGGGACTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATG
CAAGTCATTGTTTCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAG
ATCTTGGATCGCTATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGA
GCTCGCCGGCATGGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTAT
GCAATTGACCCCCAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGC
AAACTACTTGATATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAG
ATCCGGACTCCAGAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAA
GGGGCCTTGTTGGCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTT
TTGGTCAGCTACAGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAG
GCCGCATTACCCGCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCG
CCGCCGCCGCCTCCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAG
TATGAAATGCCTCAATATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATAT
GGTGAGGTGGTTGGTGAAGCTGAGGAAGAATATGAGGAGGAAGAGTGGGCAAGAAAAAGAATG
ATCAAGTTAGTTGTTGATCGAGAGTATGAAACCAGCTCAACTGGAGAAGACAGTGCTCCTGAA
TGTCAGAGAAACCGTCTTCACCATCCTAGTATCCACAGTAATATCAACGGCAATATATATATT
GCACAGAATGGTTCTGTGGTGAGAACCCGCCGTGCCTGCCTCACGGACAACTTAAAAGTTGCT
TCCCCTGTTCGACTGGGAGGGCCCTTTAAGAAACTAGACAAGTTGGCAGTGACACATGAGGAG
AATGTACCTCTGAACACATTATCAAAGGGGCCATTTTCTACTGAAAAAATGAATGCAAGACCA
ACTCTGGTTACATTTGCCCCTTGCCCTGTGGGGACTGACAATACAGCGGTGAAGCCACTAAGG
AACAGGCTGAAAAGCACAGTTGAACAGGAGTCCATGATTGACAGTAAGAACATCAAGGAGGCT
TTGGAATTTCATAGTGACCACACACAGTCTGATGATGAAGAGCTTTGGATGGGCCCCTGGAAC
AACCTCCATATACCAATGACAAAACTGTGA (SEQ ID NO: 110)

In some embodiments, the mini-PCDH15 has 8 EC domains less than the full-length PCDH15. In some examples, the mini-PCDH15 lacks EC3, EC4, EC5, EC6, EC7, EC8, EC9, and EC10 domain. In some embodiments, the mini-PCDH15 includes EC1-EC2-EC11of SEQ ID NO: 1, 53, 55, or 57. In one example, the mini-PCDH15 comprises an amino acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%

or 100% identical to SEQ ID NO: 73, 111 or 112. In some embodiments, the nucleic acid encoding the mini-PCDH15 lacking EC4, EC5, EC6, EC7, EC8, EC9, and EC10 is at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 74, 113 or 114.

An exemplary amino acid sequence of a miniPCDH15 lacking EC3, EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V10) is set forth in SEQ ID NO: 73 (mini-PCDH15 V10: includes EC1-EC2- - EC11-MAD12-TM-cyto CD1; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIK**
EGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQVIV
SNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAIDP
QTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GALL**
ALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPP
PPGAHLYEELGDSSMHNLFLLYHFQQSRGNNSVSEDRKHQQVVMPFSSNTIEAHKSAHVDGSL
KSNKLKSARKFTFLSDEDDLSAHNPLYKENISQVSTNSDISQRTDFVDPFSPKIQAKSKSLRG
PREKIQRLWSQSVSLPRRLMRKVPNRPEIIDLQQWQGTRQKAENENTGICTNKRGSSNPLLTT
EEANLTEKEEIRQGETLMIEGTEQLKSLSSDSSFCFPRPHFSFSTLPTVSRTVELKSEPNVIS
SPAECSLELSPSRPCVLHSSLSRRETPICMLPIETERNIFENFAHPPNISPSACPLPPPPPIS
PPSPPPAPAPLAPPPDISPFSLFCPPPSPPSIPLPLPPPTFFPLSVSTSGPPTPPLLPPFPTP
LPPPPPSIPCPPPPSASFLSTECVCITGVKCTTNLMPAEKIKSSMTQLSTTTVCKTDPQREPK
GILRHVKNLAELEKSVANMYSQIEKNYLRTNVSELQTMCPSEVTNMEITSEQNKGSLNNIVEG
TEKQSHSQSTSL (SEQ ID NO: 73)

An exemplary amino acid sequence of a miniPCDH15 lacking EC3, EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V10) is set forth in SEQ ID NO: 111 (mini-PCDH15 V10: includes EC1-EC2- - EC11-MAD12-TM-cyto CD2; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIK**
EGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQVIV
SNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAIDP
QTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GALL**
ALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPP

PPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEEEPKKIKKPK
VEIREPSEEEEVVVTIEKPPAAEPTYTTWKRARIFPMIFKKVRGLADKRGIVDLEGEEWQRRL
EEEDKDYLKLTLDQEEATESTVESEEESSSDYTEYSEEESEFSESETTEEESESETPSEEEES
STPESEESESTESEGEKARKNIVLARRRPMVEEVKEVKGRKEEPQEEQKEPKMEEEEHSEEEE
SGPAPVEESTDPEAQDIPEEGSAESASVEGGVESEEESESGSSSSSSESQSGGPWGYQVPAYD
RSKNANQKKSPGANSEGYNTALGALLALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARI
QAALPAAKPAVPAPAPVAAPPPPPPPPPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEE
YGEVVGEAEEEYEEEEEEPKKIKKPKVEIREPSEEEEVVVTIEKPPAAEPTYTTWKRARIFPM
IFKKVRGLADKRGIVDLEGEEWQRRLEEEDKDYLKLTLDQEEATESTVESEEESSSDYTEYSE
EESEFSESETTEEESESETPSEEEESSTPESEESESTESEGEKARKNIVLARRRPMVEEVKEV
KGRKEEPQEEQKEPKMEEEEHSEEEESGPAPVEESTDPEAQDIPEEGSAESASVEGGVESEEE
SESGSSSSSSESQSGGPWGYQVPAYDRSKNANQKKSPGANSEGYNTAL (SEQ ID NO: 111)

An exemplary amino acid sequence of a miniPCDH15 lacking EC3, EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V10) is set forth in SEQ ID NO: 112 (mini-PCDH15 V10: includes EC1-EC2- - EC11-MAD12-TM-cyto CD3; different domains alternating in bold and regular font):

MFRQFYLWTCLASGIILGSLFEICLG**QYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD**
NMLIKGTAGGPDPTIELSLKDNVDYWVLMDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCI
NKKVGTIIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPDDPTSNDTFEIPLMLTGNIVLRKRLNYEDKTRYFVIIQANDRAQNLNERRTT
TTTLTVDVLDGDDL**PPVFQKKFYIGGVSEDARMFTSVLRVKATDKDTGNYSVMAYRLIIPPIK**
EGKEGFVVETYTGLIKTAMLFHNMRRSYFKFQVIATDDYGKGLSGKADVLVSVVNQLDMQVIV
SNVPPTLVEKKIEDLTEILDRYVQEQIPGAKVVVESIGARRHGDAFSLEDYTKCDLTVYAIDP
QTNRAIDRNELFKFLDGKLLDINKDFQPYYGEGGRILEIRTPEAVTSIKKRGESLGYTE**GALL**
ALAFIIILCCIPAILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPP
PPGAHLYEELGDSSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEWARKRMIKLV
VDREYETSSTGEDSAPECQRNRLHHPSIHSNINGNIYIAQNGSVVRTRRACLTDNLKVASPVR
LGGPFKKLDKLAVTHEENVPLNTLSKGPFSTEKMNARPTLVTFAPCPVGTDNTAVKPLRNRLK
STVEQESMIDSKNIKEALEFHSDHTQSDDEELWMGPWNNLHIPMTKLGALLALAFIIILCCIP
AILVVLVSYRQFKVRQAECTKTARIQAALPAAKPAVPAPAPVAAPPPPPPPPGAHLYEELGD
SSMHKYEMPQYGSRRRLLPPAGQEEYGEVVGEAEEEYEEEEWARKRMIKLVVDREYETSSTGE
DSAPECQRNRLHHPSIHSNINGNIYIAQNGSVVRTRRACLTDNLKVASPVRLGGPFKKLDKLA
VTHEENVPLNTLSKGPFSTEKMNARPTLVTFAPCPVGTDNTAVKPLRNRLKSTVEQESMIDSK
NIKEALEFHSDHTQSDDEELWMGPWNNLHIPMTKL (SEQ ID NO: 112)

An exemplary nucleic acid sequence encoding a miniPCDH15 lacking EC3, EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V10) is set forth in SEQ ID NO: 74 (mini-PCDH15 V9: includes EC1-EC2-EC11-MAD12-TM-cyto CD1):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC

AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGCCCCCAGTGTTTCAGAAAAAA
TTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCT
ACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAA
GAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTC
CATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGA
CTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTT
TCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTGGATCGC
TATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCAT
GGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCAATTGACCCC
CAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTACTTGAT
ATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCA
GAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTG
GCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTAC
AGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCATTACCC
GCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCT
CCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAATCTTTTCCTTCTC
TACCATTTTCAACAAAGCAGGGGAAATAACTCAGTCTCAGAAGACAGGAAACATCAACAAGTT
GTGATGCCCTTTTCTTCCAATACTATTGAGGCTCACAAGTCAGCTCATGTAGACGGATCACTT
AAGAGCAACAAACTGAAGTCTGCAAGAAAATTCACATTTCTATCTGATGAGGATGACTTAAGT
GCCCATAATCCCCTTTATAAGGAAAACATAAGTCAAGTATCAACAAATTCAGACATTTCACAG
AGAACAGATTTTGTAGACCCATTTTCACCCAAAATACAAGCCAAGAGTAAGTCTCTGAGGGGC
CCAAGAGAAAAGATTCAGAGGCTGTGGAGTCAGTCAGTCAGCTTACCCAGGAGGCTGATGAGG
AAAGTTCCAAATAGACCAGAGATCATAGATCTGCAGCAGTGGCAAGGCACCAGGCAGAAAGCT
GAAAATGAAAACACTGGAATCTGTACAAACAAAAGAGGTAGCAGCAATCCATTGCTTACAACT
GAAGAGGCAAATTTGACAGAGAAAGAGGAAATAAGGCAAGGTGAAACACTGATGATAGAAGGA
ACAGAACAGTTGAAATCTCTCTCTTCAGACTCTTCATTTTGCTTTCCCAGGCCTCACTTCTCA
TTCTCCACTTTGCCAACTGTTTCAAGAACTGTGGAACTCAAATCAGAACCTAATGTCATCAGT
TCTCCTGCTGAGTGTTCCTTGGAACTTTCTCCTTCAAGGCCTTGTGTTTTACATTCTTCACTC
TCTAGGAGAGAGACACCTATTTGTATGTTACCTATTGAAACCGAAAGAAATATTTTTGAAAAT
TTTGCCCATCCACCAAACATCTCTCCTTCTGCCTGTCCCCTTCCCCCTCCTCCTCCTATTTCT
CCTCCTTCTCCTCCTCCTGCTCCTGCTCCTCTTGCTCCTCCTCCTGACATTTCTCCTTTTTCT
CTTTTTTGTCCTCCTCCCTCTCCTCCTTCTATCCCTCTTCCTCTTCCTCCTCCTACATTTTTT
CCACTTTCCGTTTCAACGTCTGGTCCCCCAACACCACCTCTTCTACCTCCATTTCCAACTCCT
CTTCCTCCACCACCTCCTTCTATTCCTTGCCCTCCACCTCCTTCAGCTTCATTTCTGTCCACA
GAGTGTGTCTGTATAACAGGTGTTAAATGCACGACCAACTTGATGCCTGCCGAGAAAATTAAG
TCCTCTATGACACAGCTATCAACAACGACAGTGTGTAAAACAGACCCTCAGAGAGAACCAAAA
GGCATCCTCAGACACGTTAAAAACTTAGCAGAACTTGAAAAATCAGTAGCTAACATGTACAGT
CAAATAGAAAAAAACTATCTACGCACAAATGTTTCAGAACTTCAAACTATGTGCCCTTCAGAA

GTAACAAATATGGAAATCACATCTGAACAAAACAAGGGGAGTTTGAACAATATTGTCGAGGGA
ACTGAAAAACAATCTCACAGTCAATCTACTTCACTGTAA (SEQ ID NO: 74)

An exemplary nucleic acid sequence encoding a miniPCDH15 lacking EC3, EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V10) is set forth in SEQ ID NO: 113 (mini-PCDH15 V9: includes EC1-EC2-EC11-MAD12-TM-cyto CD2):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGCCCCCAGTGTTTCAGAAAAAA
TTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCT
ACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAA
GAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTC
CATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGA
CTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTT
TCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTGGATCGC
TATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCAT
GGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCAATTGACCCC
CAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTACTTGAT
ATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCA
GAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTG
GCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTAC
AGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCATTACCC
GCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCT
CCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAGTATGAAATGCCT
CAATATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATATGGTGAGGTGGTT
GGTGAAGCTGAGGAAGAATATGAGGAGGAAGAGGAAGAGCCAAAGAAAATTAAAAAACCAAAG
GTTGAAATTAGAGAGCCTAGTGAGGAGGAAGAAGTAGTTGTAACTATCGAAAAACCACCAGCA
GCTGAGCCTACATACACAACATGGAAGAGAGCCAGAATATTCCCCATGATTTTTAAGAAAGTT
AGAGGATTAGCTGATAAAAGAGGAATCGTTGACCTTGAGGGTGAAGAGTGGCAGAGACGCCTT
GAGGAAGAAGATAAAGATTATTTGAAACTCACTCTGGACCAAGAGGAAGCAACAGAAAGCACT
GTAGAATCAGAGGAGGAATCCTCCAGCGACTATACTGAATACAGTGAAGAAGAGTCTGAGTTC
AGTGAGTCTGAGACTACAGAAGAGGAATCTGAGTCAGAGACACCCTCTGAGGAGGAGGAGAGT
TCCACCCCTGAATCAGAAGAATCGGAATCCACAGAGTCAGAAGGAGAAAAAGCAAGGAAAAAC
ATTGTGCTTGCAAGAAGAAGGCCCATGGTTGAGGAGGTCAAGGAAGTCAAGGGTAGGAAAGAG
GAGCCACAAGAAGAACAAAAAGAACCTAAGATGGAAGAAGAAGAACACTCAGAAGAAGAAGAA

AGTGGACCAGCCCCTGTGGAAGAAAGTACAGACCCTGAAGCTCAAGATATCCCTGAAGAGGGC
AGTGCAGAATCAGCTTCGGTGGAAGGAGGTGTGGAAAGTGAGGAGGAATCAGAATCAGGTAGT
AGTAGCAGTAGTAGCGAAAGTCAGTCTGGAGGTCCATGGGGCTATCAGGTACCAGCGTATGAC
AGAAGCAAGAATGCAAACCAAAAGAAGTCGCCAGGAGCAAACTCTGAAGGTTACAACACAGCA
CTTTGA (SEQ ID NO: 113)

An exemplary nucleic acid sequence encoding a miniPCDH15 lacking EC3, EC4, EC5, EC6, EC7, EC8, EC9, and EC10 (V10) is set forth in SEQ ID NO: 114 (mini-PCDH15 V9: includes EC1-EC2-EC11-MAD12-TM-cyto CD3):

ATGTTTCGACAGTTTTATCTCTGGACATGTTTAGCTTCAGGGATCATCCTGGGCTCTCTCTTT
GAAATCTGCTTGGGCCAGTATGATGATGACTGGCAATATGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACCATAGTTGCTATTGATGAAGAAAGTCGGAATGGTACAATTCTGGTGGAC
AACATGCTGATCAAAGGGACTGCTGGAGGACCAGACCCCACCATAGAACTTTCTTTAAAGGAT
AATGTGGATTACTGGGTGTTGATGGATCCTGTTAAGCAAATGCTTTTCCTGAACAGCACCGGA
AGAGTTCTGGATAGAGATCCACCGATGAACATACACTCCATTGTGGTGCAGGTCCAGTGCATC
AACAAAAAAGTGGGCACTATTATCTACCATGAAGTGCGAATAGTGGTGAGAGACAGGAATGAC
AACTCACCCACTTTCAAGCATGAAAGCTACTATGCCACAGTGAATGAGCTCACTCCAGTTGGT
ACCACAATATTCACAGGATTTTCAGGAGACAATGGAGCTACAGATATAGATGATGGACCAAAT
GGACAGATAGAGTATGTTATTCAGTATAATCCAGATGATCCGACATCCAATGACACCTTTGAA
ATTCCCCTAATGTTGACTGGAAATATAGTGTTAAGGAAGAGGCTCAACTATGAAGATAAGACT
CGCTACTTTGTCATAATCCAAGCTAATGACCGTGCCCAAAATCTGAATGAGAGGCGAACCACC
ACCACCACTCTCACAGTGGATGTTCTGGATGGAGATGACTTGCCCCCAGTGTTTCAGAAAAAA
TTCTACATCGGAGGTGTATCTGAAGATGCAAGAATGTTTACTTCTGTACTCAGAGTGAAGGCT
ACTGATAAAGATACTGGCAATTATAGTGTCATGGCCTACAGACTCATAATACCACCAATTAAA
GAGGGAAAAGAAGGATTTGTAGTGGAAACATATACAGGGCTTATCAAAACTGCTATGCTCTTC
CATAATATGAGGAGATCCTACTTCAAGTTTCAAGTTATTGCAACTGACGACTATGGGAAGGGA
CTGAGCGGCAAAGCCGATGTACTCGTCTCCGTGGTCAATCAGCTGGATATGCAAGTCATTGTT
TCCAATGTGCCTCCTACTCTAGTGGAAAAAAAGATAGAAGATCTTACAGAGATCTTGGATCGC
TATGTTCAGGAACAAATTCCTGGTGCCAAGGTCGTAGTGGAGTCCATTGGAGCTCGCCGGCAT
GGAGATGCCTTTTCCCTAGAAGATTACACCAAATGTGACTTGACTGTCTATGCAATTGACCCC
CAAACCAACAGAGCCATCGATAGAAATGAGCTTTTTAAATTTTTGGATGGCAAACTACTTGAT
ATCAATAAAGACTTTCAGCCGTATTATGGGGAAGGAGGACGCATTCTGGAGATCCGGACTCCA
GAGGCAGTGACCAGCATTAAAAAGAGAGGAGAAAGTCTAGGATACACAGAAGGGGCCTTGTTG
GCTCTGGCCTTCATCATCATCCTCTGCTGCATTCCTGCCATCTTGGTGGTTTTGGTCAGCTAC
AGACAGTTTAAAGTACGTCAAGCTGAGTGTACAAAGACTGCACGAATTCAGGCCGCATTACCC
GCGGCTAAACCAGCAGTGCCGGCTCCTGCACCAGTGGCAGCGCCCCCGCCGCCGCCGCCGCCT
CCGCCAGGTGCGCATCTCTATGAAGAACTTGGAGACAGCTCAATGCATAAGTATGAAATGCCT
CAATATGGGAGTCGCCGTCGATTGTTACCACCAGCTGGACAGGAGGAATATGGTGAGGTGGTT
GGTGAAGCTGAGGAAGAATATGAGGAGGAAGAGTGGGCAAGAAAAAGAATGATCAAGTTAGTT
GTTGATCGAGAGTATGAAACCAGCTCAACTGGAGAAGACAGTGCTCCTGAATGTCAGAGAAAC
CGTCTTCACCATCCTAGTATCCACAGTAATATCAACGGCAATATATATATTGCACAGAATGGT
TCTGTGGTGAGAACCCGCCGTGCCTGCCTCACGGACAACTTAAAAGTTGCTTCCCCTGTTCGA
CTGGGAGGGCCCTTTAAGAAACTAGACAAGTTGGCAGTGACACATGAGGAGAATGTACCTCTG
AACACATTATCAAAGGGGCCATTTTCTACTGAAAAAATGAATGCAAGACCAACTCTGGTTACA
TTTGCCCCTTGCCCTGTGGGGACTGACAATACAGCGGTGAAGCCACTAAGGAACAGGCTGAAA
AGCACAGTTGAACAGGAGTCCATGATTGACAGTAAGAACATCAAGGAGGCTTTGGAATTTCAT

AGTGACCACACACAGTCTGATGATGAAGAGCTTTGGATGGGCCCCTGGAACAACCTCCATATA CCAATGACAAAACTGTGA (SEQ ID NO: 114)

In a full-length PCDH15 protein, the last five amino acids of an EC domain immediately preceding the next EC domain is the linking region between the two EC domains (linkers). Depending on the amino acid sequences of these linkers, they can be flexible or rigid. Some linkers may have different calcium ion binding capacities (e.g., from 0 to 3 Ca^{2+}). The presence, absence, or quantity of the Ca^{2+} may be important for proper function of the PCDH15. Linkers between the EC domains of PCDH15 have been previously described (e.g., Sotomayor et al, A partial calcium-free linker confers flexibility to inner-ear protocadherin-15, *Structure.* 2017 Mar 7; 25(3): 482–495.) Due to the deletion of certain EC domains in mini-PCDH15, some EC domains are connected artificially, and the succeeding EC domain is connected to the preceding one with a linker different from a full-length PCDH15. For example, in mini-PCDH15 V1, EC3 is connected with EC5, and the linker sequence is the last five amino acids of EC3 (DENNQ), as opposed to the situation in a full-length PCDH15, where EC5 is connected to EC4 with the last five amino acids of EC4 (DANDN).

In some embodiments, when connecting two EC domains that are not connected in a wild type PCDH15 (e.g., EC3 connected to EC5 in mini-PCDH15 V1 and V5, EC4 connected to EC8 in mini-PCDH15 V2, EC3 connected to EC8 in mini-PCDH15 V3, EC7 connected to EC11 in mini-PCDH15 V5 and V8, EC4 connected to EC7 in mini-PCDH15 V6 and V8, EC8 connected to EC11 in mini-PCDH15 V6 and V7, EC3 connected to EC9 in mini-PCDH15 V4, EC3 connected to EC7 in mini-PCDH15 V7, EC3 connected to EC11 in mini-PCDH15 V9, and EC2 connected to EC11 in mini-PCDH15 V10), the linking region may or may not affect the function of the miniPCDH15. One skilled in the art would understand that any of the EC domains of PCDH15 may be artificially connected to another EC domain in engineering of the mini-PCDH15.

Non-limiting examples of linkers between the EC domains artificially connected in the mini-PCDH15 are shown in the Table 2 below:

1. EC3-EC5 (V1, V5); native linker on EC3 (DENNQ (SEQ ID NO: 121)) is used vs EC4's DANDN (SEQ ID NO: 122);
2. EC6-EC9 (V1); native linker on EC6 (DVNDN (SEQ ID NO: 123)) is used vs EC8's DMNDY (SEQ ID NO: 124);
3. EC4-EC8 (V2); native linker on EC4 (DANDN (SEQ ID NO: 122)) is used vs EC7's DIDDN (SEQ ID NO: 125);

4. EC3-EC8 (V3); native linker on EC3 (DENNQ (SEQ ID NO: 121)) is used vs EC7's DIDDN (SEQ ID NO: 125);
5. EC3-EC9 (V4); native linker on EC3 (DENNQ (SEQ ID NO: 121)) is used vs EC8's DMNDY (SEQ ID NO: 124);
6. EC7-EC11 (V5, V8); native linker on EC7 (DIDDN (SEQ ID NO: 125)) is used vs EC10's DENNH (SEQ ID NO: 126);
7. EC4-EC7 (V6, V8); native linker on EC4 (DANDN (SEQ ID NO: 122)) is used vs EC6's DVNDN (SEQ ID NO: 123);
8. EC8-EC11 (V6, V7); native linker on EC8 (DMNDY (SEQ ID NO: 124)) is used vs EC10's DENNH (SEQ ID NO: 126);
9. EC3-EC11 (V9); native linker on EC3 (DENNQ (SEQ ID NO: 121)) is used vs EC10's DENNH (SEQ ID NO: 126);
10. EC2-EC11 (V10); native linker on EC2 (DGDDL (SEQ ID NO: 127)) is used vs EC10's DENNH (SEQ ID NO: 126);
11. EC3-EC7 (V7); native linker on EC3 (DENNQ(SEQ ID NO: 121)) is used vs EC6's DVNDN (SEQ ID NO: 123)

In some embodiments, in mini-PCDH15 V1, the linker between EC3 and EC5 is the last five amino acids of EC3 (DENNQ (SEQ ID NO: 121)), and/or the linker between EC6 and EC9 is the last five amino acids of EC6 (DVNDN (SEQ ID NO: 123)). In some embodiment, in mini-PCDH15 V2, the linker between EC4 and EC8 is the last five amino acids of EC4 (DANDN (SEQ ID NO: 122)). In some embodiment, in mini-PCDH15 V3, the linker between EC3 and EC8 is the last five amino acids of EC3 (DENNQ (SEQ ID NO: 121)). In some embodiment, in mini-PCDH15 V5, the linker between EC3 and EC5 is the last five amino acids of EC3 (DENNQ (SEQ ID NO: 121)), and/or the linker between EC7 and EC11 is the last five amino acids of EC7 (DIDDN (SEQ ID NO: 125)). In some embodiment, in mini-PCDH15 V6, the linker between EC4 and EC7 is the last five amino acids of EC4 (DANDN (SEQ ID NO: 122)), and/or the linker between EC8 and EC11 is the last five amino acids of EC8 (DMNDY (SEQ ID NO: 124)). In some embodiment, in mini-PCDH15 V4, the linker between EC3 and EC9 is the last five amino acids of EC3 (DENNQ (SEQ ID NO: 121)). In some embodiment, in mini-PCDH15 V7, the linker between EC3 and EC7 is the last five amino acids of EC3 (DENNQ (SEQ ID NO: 121)), and/or the linker between EC8 and EC11 is the last five amino acids of EC8 (DMNDY (SEQ ID NO: 124)). In some embodiment, in mini-PCDH15 V8, the linker between EC4 and EC7 is the last five amino acids of EC4 (DANDN (SEQ ID NO: 122)), and/or the linker between EC7 and EC11 is the last five amino acids of EC7 (DIDDN (SEQ ID NO: 125)). In some embodiment, in mini-PCDH15 V9, the linker

between EC3 and EC11 is the last five amino acids of EC3 (DENNQ (SEQ ID NO: 121)). In some embodiment, in mini-PCDH15 V10, the linker between EC2 and EC11 is the last five amino acids of EC2 (DGDDL (SEQ ID NO: 127)).

In some embodiments, these linkers between the EC domains can be further modified to confer desired effect with respect to the function of the mini-PCDH15. In some embodiments, the linkers can be altered to alter its flexibility. In some embodiments, the linkers can be altered to confer calcium binding capacities. In some embodiments, some of the amino acid residues of the linkers can be replaced by amino acids S, A, G, or N, or amino acids S, A, G, or N can be added to the linker sequence to alter flexibility. In some embodiments, a chimeric linker may be formed (e.g., to link EC3 and EC5, a chimeric linker between EC3 linker and EC4 linker can be engineered). In some embodiments, any of the mini-PCDH15 described herein may have altered linker sequence replacing the current linker sequences connecting the EC domains. Non-limiting examples of possible linkers between the artificially connected domains are shown in Table 3 below. It is known in the art that the second amino acid is not conserved and may not be crucial to linker function, therefore the second amino acid residual of the linker are shown as X, which can be any amino acid (e.g., R, G, E, A, P, V, I, M, P, E, V, or Q).

SEQ ID NO:	**EC**	**Linker**					**EC**	**V# Version?**
130		D	X	N	D	N		
1. EC3-EC5 (V1, V5); native linker on EC3 (DENNQ (SEQ ID NO: 121)) is used vs EC4's DANDN (SEQ ID NO: 122);								
121	EC3	D	E	N	N	Q	EC5	V1, V5
128		D	X	N	D	Q		
129		D	X	N	N	Q		
130		D	X	N	D	N		
122		D	A	N	D	N		
2. EC6-EC9 (V1); native linker on EC6 (DVNDN (SEQ ID NO: 123)) is used vs EC8's DMNDY (SEQ ID NO: 124);								
123	EC6	D	V	N	D	N	EC9	V1
131		D	X	N	D	Y		
130		D	X	N	D	N		
124		D	M	N	D	Y		

3. EC4-EC8 (V2); native linker on EC4 (DANDN (SEQ ID NO: 122)) is used vs EC7's DIDDN (SEQ ID NO: 125);								
122	EC4	D	A	N	D	N	EC8	V2
132		D	X	D	D	N		
125		D	I	D	D	N		
4. EC3-EC8 (V3); native linker on EC3 (DENNQ (SEQ ID NO: 121)) is used vs EC7's DIDDN (SEQ ID NO: 125);								
121	EC3	D	E	N	N	Q	EC8	V3
129		D	X	N	N	Q		
130		D	X	N	D	N		
133		D	X	N	N	N		
128		D	X	N	D	Q		
125		D	I	D	D	N		
5. EC3-EC9 (V4); native linker on EC3 (DENNQ (SEQ ID NO: 121)) is used vs EC8's DMNDY (SEQ ID NO: 124);								
121	EC3	D	E	N	N	Q	EC9	V4
128		D	X	N	D	Q		
130		D	X	N	D	N		
131		D	X	N	D	Y		
124		D	M	N	D	Y		
6. EC7-EC11 (V5, V8); native linker on EC7 (DIDDN (SEQ ID NO: 125)) is used vs EC10's DENNH (SEQ ID NO: 126);								
125	EC7	D	I	D	D	N	EC11	V5, V8
130		D	X	N	D	N		
133		D	X	N	N	N		
134		D	X	N	N	H		
135		D	X	D	N	H		
126		D	E	N	N	H		
7. EC4-EC7 (V6, V8); native linker on EC4 (DANDN (SEQ ID NO: 122)) is used vs EC6's DVNDN (SEQ ID NO: 123);								
122	EC4	D	A	N	D	N	EC7	V6, V8
130		D	X	N	D	N		
123		D	V	N	D	N		
8. EC8-EC11 (V6, V7); native linker on EC8 (DMNDY (SEQ ID NO: 124)) is used vs EC10's DENNH (SEQ ID NO: 126);								
124	EC8	D	M	N	D	Y	EC11	V6, V7
130		D	X	N	D	N		
136		D	X	N	N	Y		
133		D	X	N	N	N		
134		D	X	N	N	H		
131		D	X	N	D	Y		
126		D	E	N	N	H		

9. EC3-EC11 (V9); native linker on EC3 (DENNQ (SEQ ID NO: 121)) is used vs EC10's DENNH (SEQ ID NO: 126);								
121	EC3	D	E	N	N	Q	EC11	V9
126		D	E	N	N	H		
10. EC2-EC11 (V10); native linker on EC2 (DGDDL (SEQ ID NO: 127)) is used vs EC10's DENNH (SEQ ID NO: 126);								
127	EC2	D	G	D	D	L	EC11	V10
130		D	X	N	D	N		
133		D	X	N	N	N		
137		D	X	N	N	L		
138		D	X	N	D	L		
126		D	E	N	N	H		
11. EC3-EC7 (V7); native linker on EC3 (DENNQ(SEQ ID NO: 121)) is used vs EC6's DVNDN (SEQ ID NO: 123)								
121	EC3	D	E	N	N	Q	EC7	V7
130		D	X	N	D	N		
133		D	X	N	N	N		
128		D	X	N	D	Q		
123		D	V	N	D	N		

In some embodiments, any of the known linkers can be used in connecting the EC domains of a miniPCDH15. Non-limiting examples of known linkers include: GGGSGGG (SEQ ID NO: 139), GGSGG (SEQ ID NO: 140), DGNDN (SEQ ID NO: 141), DGNNN (SEQ ID NO: 142), DANDN (SEQ ID NO: 122), DANNN(SEQ ID NO: 143), GGNDN(SEQ ID NO: 144), GGNNN(SEQ ID NO: 145), GGSNN(SEQ ID NO: 146), GGSAA(SEQ ID NO: 147), AANDN(SEQ ID NO: 148), AANNN(SEQ ID NO: 149).

In some embodiments, the transgenes encoding a mini-PCDH15 described by the disclosure mediate cell adhesion by binding to CDH23 at its N-terminal. PCDH15 is a component of tip links, which gate mechanotransduction channels. The PCDH15 C-terminal (cytoplasmic domain) can bind to transmembrane channel like 1 (TMC1) and LHFPL Tetraspan Subfamily Member 5 (LHFPL5). Mutations in PCDH15 have been identified to be related to hereditary hearing loss and/or blindness, for example, Usher Syndrome type 1F. Generally, Usher syndrome refers to a condition characterized by partial or total hearing loss and vision loss that worsens over time. The hearing loss is classified as sensorineural, which means that it is caused by abnormalities of the inner ear. The loss of vision is caused by an eye disease called retinitis pigmentosa (RP), which affects the layer of light-sensitive tissue at the

back of the eye (the retina). There are three major types of Usher syndrome, designated as types I, II, and III. These types are distinguished by the severity of hearing loss, the presence or absence of balance problems, and the age at which signs and symptoms appear. The types are further divided into subtypes based on their genetic cause. Usher syndrome type 1F is an inherited disease that causes profound hearing loss from birth and impairs vision beginning in adolescence. Usher Syndrome type 1F is caused by mutations in *PCDH15* gene encoding PCDH15.

Generally, ITR sequences are about 145 bp in length. Preferably, substantially the entire sequences encoding the ITRs are used in the molecule, although some degree of minor modification of these sequences is permissible. The ability to modify these ITR sequences is within the skill of the art. (See, *e.g.*, texts such as Sambrook *et al.*, *Molecular Cloning. A Laboratory Manual*, 2d ed., Cold Spring Harbor Laboratory, New York (1989); and K. Fisher *et al.*, *J. Virol.*, 70:520 532 (1996)). An example of such a molecule employed in the present invention is a "cis-acting" plasmid containing the transgene, in which the selected transgene sequence and associated regulatory elements are flanked by the 5' and 3' AAV ITR sequences. The AAV ITR sequences may be obtained from any known AAV, including presently identified mammalian AAV types. In some embodiments, the isolated nucleic acid comprises at least one ITR having a serotype selected from AAV1, AAV2, AAV5, AAV6, AAV6.2, AAV7, AAV8, AAV9, AAV10, and AAV11. In some embodiments, the isolated nucleic acid comprises a region (*e.g.*, a first region) encoding an AAV2 ITR. In some embodiments, the isolated nucleic acid comprises a transgene (*e.g.*, mini-PCDH15) flanked by AAV ITRs (e.g., AAV2 ITR)

In some embodiments, the isolated nucleic acid further comprises a region (*e.g.*, a second region, a third region, a fourth region, *etc.*) comprising a second AAV ITR. In some embodiments, the second AAV ITR has a serotype selected from AAV1, AAV2, AAV5, AAV6, AAV6.2, AAV7, AAV8, AAV9, AAV10, AAV11, and variants thereof. In some embodiments, the second ITR is a mutant ITR that lacks a functional terminal resolution site (TRS). The term “lacking a terminal resolution site” can refer to an AAV ITR that comprises a mutation (*e.g.*, a sense mutation such as a non-synonymous mutation, or missense mutation) that abrogates the function of the terminal resolution site (TRS) of the ITR, or to a truncated AAV ITR that lacks a nucleic acid sequence encoding a functional TRS (*e.g.*, a ΔTRS ITR).

Without wishing to be bound by any particular theory, a rAAV vector comprising an ITR lacking a functional TRS produces a self-complementary rAAV vector, for example, as described by McCarthy (2008) *Molecular Therapy* 16(10):1648-1656. Any referenced cited in the present disclosure are incorporated by reference in its entirety.

The isolated nucleic acid as described herein, may be incorporated into a vector. In addition to the major elements identified above for the recombinant AAV vector, the vector also includes conventional control elements which are operably linked with elements of the transgene in a manner that permits its transcription, translation, and/or expression in a cell transfected with the vector or infected with the virus produced by the invention. As used herein, "operably linked" sequences include both expression control sequences that are contiguous with the gene of interest and expression control sequences that act in trans or at a distance to control the gene of interest. Expression control sequences include appropriate transcription initiation, termination, promoter, and enhancer sequences; efficient RNA processing signals such as splicing and polyadenylation (polyA) signals; sequences that stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (*i.e.*, Kozak consensus sequence); sequences that enhance protein stability; and when desired, sequences that enhance secretion of the encoded product. A number of expression control sequences, including promoters which are native, constitutive, inducible and/or tissue-specific, are known in the art and may be utilized. In some embodiments, the transgene comprises a Kozak consensus sequence at the 5′ end of the nucleic acid sequence encoding the transgene (*e.g.*, *mini-PCDH15*).

As used herein, a nucleic acid sequence (*e.g.*, coding sequence) and regulatory sequences are said to be operably linked when they are covalently linked in such a way as to place the expression or transcription of the nucleic acid sequence under the influence or control of the regulatory sequences. If it is desired that the nucleic acid sequences be translated into a functional protein, two DNA sequences are said to be operably linked if induction of a promoter in the 5′ regulatory sequences results in the transcription of the coding sequence and if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region to direct the transcription of the coding sequences, or (3) interfere with the ability of the corresponding RNA transcript to be translated into a protein. Thus, a promoter region would

be operably linked to a nucleic acid sequence if the promoter region were capable of effecting transcription of that DNA sequence such that the resulting transcript might be translated into the desired protein or polypeptide. Similarly two or more coding regions are operably linked when they are linked in such a way that their transcription from a common promoter results in the expression of two or more proteins having been translated in frame. In some embodiments, operably linked coding sequences yield a fusion protein.

A "promoter" refers to a DNA sequence recognized by the synthetic machinery of the cell, or introduced synthetic machinery, required to initiate the specific transcription of a gene. The phrases "operatively positioned," "under control," or "under transcriptional control" means that the promoter is in the correct location and orientation in relation to the nucleic acid to control RNA polymerase initiation and expression of the gene.

Examples of constitutive promoters include, without limitation, the retroviral Rous sarcoma virus (RSV) LTR promoter (optionally with the RSV enhancer), the cytomegalovirus (CMV) promoter (optionally with the CMV enhancer) [see, *e.g.*, Boshart *et al.*, Cell, 41:521-530 (1985)], the SV40 promoter, the dihydrofolate reductase promoter, the β-actin promoter, the phosphoglycerol kinase (PGK) promoter, and the EF1α promoter [Invitrogen]. In some embodiments, a promoter is hybrid cytomegalovirus (CMV) immediate-early/Chicken beta-actin promoter (CAG promoter). In some embodiments, a promoter is a chicken beta-actin (CBA) promoter. In some embodiments, the promoter is a minimal promoter. A minimal promoter is a part of promoter located between -35 to +35 region with respect to transcription start site. It has one or more of 3 conservative sequence i.e. Tata box, initiator region, binding site for RNA polymerase and downstream promoter element. Exemplary minimal promoters can be less than 400, 400, 200, 195, 190, 185, 180 or less nucleotides in length. In some examples, the minimal promoter is a minimal CMV promoter (*e.g.*, CMV584 promoter bp promoter). In other examples, the minimal promoter is a JeT promoter.

An exemplary nucleic acid sequence for CMV584 bp promoter is set forth in SEQ ID NO: 115:

GACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCAT
ATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACC
CCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATT
GACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATA
TGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGT
ACATGACCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCA

TGGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTC
CAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTC
CAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGG
TCTATATAAGCAGAGCT (SEQ ID NO: 115)

Inducible promoters allow regulation of gene expression and can be regulated by exogenously supplied compounds, environmental factors such as temperature, or the presence of a specific physiological state, *e.g.*, acute phase, a particular differentiation state of the cell, or in replicating cells only. Inducible promoters and inducible systems are available from a variety of commercial sources, including, without limitation, Invitrogen, Clontech and Ariad. Many other systems have been described and can be readily selected by one of skill in the art. Examples of inducible promoters regulated by exogenously supplied promoters include the zinc-inducible sheep metallothionine (MT) promoter, the dexamethasone (Dex)-inducible mouse mammary tumor virus (MMTV) promoter, the T7 polymerase promoter system (WO 98/10088); the ecdysone insect promoter (No *et al.*, *Proc. Natl. Acad. Sci. USA*, 93:3346-3351 (1996)), the tetracycline-repressible system (Gossen *et al.*, *Proc. Natl. Acad. Sci. USA*, 89:5547-5551 (1992)), the tetracycline-inducible system (Gossen *et al.*, Science, 268:1766-1769 (1995), see also Harvey *et al.*, *Curr. Opin. Chem. Biol.*, 2:512-518 (1998)), the RU486-inducible system (Wang *et al.*, *Nat. Biotech.*, 15:239-243 (1997) and Wang *et al.*, *Gene Ther.*, 4:432-441 (1997)) and the rapamycin-inducible system (Magari *et al.*, *J. Clin. Invest.*, 100:2865-2872 (1997)). Still other types of inducible promoters which may be useful in this context are those which are regulated by a specific physiological state, *e.g.*, temperature, acute phase, a particular differentiation state of the cell, or in replicating cells only.

In another embodiment, the native promoter for the transgene will be used. The native promoter may be preferred when it is desired that expression of the transgene should mimic the native expression. The native promoter may be used when expression of the transgene must be regulated temporally or developmentally, or in a tissue-specific manner, or in response to specific transcriptional stimuli. In a further embodiment, other native expression control elements, such as enhancer elements, polyadenylation sites or Kozak consensus sequences may also be used to mimic the native expression. In some embodiments, the promoter is a native promoter. In some examples, the promoter can drive the transgene expression (*e.g.*, mini-PCDH15) in the cells of the eye (*e.g.*, rods, cones, horizontal cells, bipolar cells, and muller glias, etc) (Angueyra et al., Leveraging Zebrafish to Study Retinal Degeneration, *Front Cell*

Dev Biol. 2018; 6: 110). Non-limiting exemplary native promoters can be a Methyl-CpG Binding Protein 2 (MeCP2) promoter, a Ubiquitin-C (UbiC) promoter, a Bestrophin 1 (Best1) (retina native) promoter, a human red opsin (RedO) promoter, a human rhodopsin kinase (RK) promoter, a mouse cone arrestin (CAR) promoter, a human rhodopsin (Rho) promoter, a UV opsin-specific 1 (opn1sw1) promoter, a UV opsin-specific 2 (opn1sw2) promoter, an Opsin 1, Medium Wave Sensitive 2 (opn1mw2) promoter, an opsin 1, long-wave-sensitive 1 (opn1lw1) promoter, a blue cone specific promoter (sws2), an L-opsin (opn1lw1-cxxc1) promoter, a thyroid hormone receptor β (thrb) promoter, an LIM Homeobox 1a (lhx1a) promoter, a connexin 55.5 (cx55.5) promoter, a metabotropic glutamate receptor 6b (grm6b), a glial fibrillar acidic protein (gfap) promoter, a cone transducin alpha subunit (gnat2)promoter, a connexin 52.7 (cx52.7) promoter, a connexin 52.9 (cx52.9) promoter, a heat shock cognate 70-kd protein,-like (hsp70l) promoter, a yeast transcription activator protein- (GAL4-VP16) promoter, a upstream activation sequence (UAS), a visual system homeobox 1 (vsx1) promoter, or a rhodopsin (zop) promoter.

For nucleic acids encoding proteins, a polyadenylation sequence generally is inserted following the transgene sequences and before the 3′ AAV ITR sequence. A rAAV construct useful in the present disclosure may also contain an intron, desirably located between the promoter/enhancer sequence and the transgene. One possible intron sequence is derived from SV-40, and is referred to as the SV-40 T intron sequence. Another vector element that may be used is an internal ribosome entry site (IRES). An IRES sequence is used to produce more than one polypeptide from a single gene transcript. An IRES sequence would be used to produce a protein that contain more than one polypeptide chains. Selection of these and other common vector elements are conventional and many such sequences are available [see, *e.g.*, Sambrook *et al.*, and references cited therein at, for example, pages 3.18 3.26 and 16.17 16.27 and Ausubel *et al.*, Current Protocols in Molecular Biology, John Wiley & Sons, New York, 1989]. In some embodiments, a Foot and Mouth Disease Virus 2A sequence is included in polyprotein; this is a small peptide (approximately 18 amino acids in length) that has been shown to mediate the cleavage of polyproteins (Ryan, M D *et al.*, EMBO, 1994; 4: 928-933; Mattion, N M *et al.*, J Virology, November 1996; p. 8124-8127; Furler, S *et al.*, Gene Therapy, 2001; 8: 864-873; and Halpin, C *et al.*, The Plant Journal, 1999; 4: 453-459). The cleavage activity of the 2A sequence has previously been demonstrated in artificial systems including

plasmids and gene therapy vectors (AAV and retroviruses) (Ryan, M D *et al.*, EMBO, 1994; 4: 928-933; Mattion, N M *et al.*, J Virology, November 1996; p. 8124-8127; Furler, S *et al.*, Gene Therapy, 2001; 8: 864-873; and Halpin, C *et al.*, The Plant Journal, 1999; 4: 453-459; de Felipe, P *et al.*, Gene Therapy, 1999; 6: 198-208; de Felipe, P *et al.*, Human Gene Therapy, 2000; 11: 1921-1931.; and Klump, H *et al.*, Gene Therapy, 2001; 8: 811-817).

In some embodiments, the regulatory sequences impart tissue-specific gene expression capabilities. In some cases, the tissue-specific regulatory sequences bind tissue-specific transcription factors that induce transcription in a tissue specific manner. Such tissue-specific regulatory sequences (*e.g.*, promoters, enhancers, *etc.*) are well known in the art. In some embodiments, the tissue-specific promoter is an eye-specific promoter. Examples of eye-specific promoters include but are not limited to a retinoschisin promoter, K12 promoter, a rhodopsin promoter, a rod-specific promoter, a cone-specific promoter, a rhodopsin kinase promoter, a GRK1 promoter, an interphotoreceptor retinoid-binding protein proximal (IRBP) promoter, and an opsin promoter (*e.g.*, a red opsin promoter, a blue opsin promoter, *etc.*). In some embodiments, the tissue-specific promoter is an inner ear cell-specific promoter. Examples of inner ear cell-specific promoters include but are not limited to Myosin 7 promoter, Myosin 15 promoter, TMC1 promoter.

The present disclosure, provides isolated nucleic acids and/or vectors (*e.g.,* AAV vectors) for expressing a transgene (*e.g., mini-PCDH15*), such isolated nucleic acids and/or vectors include AAV LTRs (*e.g.,* AAV2 LTRs) and a transgene operably linked to a promoter (*e.g.,* chicken beta actin promoter or a minimal promoter). In addition, the vector can further comprise certain regulatory elements (*e.g.,* enhancers, kozak sequences, Woodchuck Hepatitis Virus (WHP) Posttranscriptional Regulatory Element (WPRE) and poly adenylation sites (*e.g.*, bovine growth hormone polyadenylation (bgh-PolyA) signal)). In some embodiments, the isolated nucleic acids and/or vectors does not comprise a WPRE. In some embodiments, the isolated nucleic acids and/or vectors comprise a WPRE. In some embodiments, the isolated nucleic acids and/or vectors comprise a BGH signal. In some embodiments, the isolated nucleic acids and/or vectors comprise AAV2 ITR flanking CMV584bp promoter operably linked to a transgene (*e.g.*, mini-PCDH15), no WPRE and BGH poly (A).

II. Recombinant Adeno-Associated Viruses (rAAVs)

In some aspects, the disclosure provides isolated AAVs. As used herein with respect to AAVs, the term "isolated" refers to an AAV that has been artificially produced or obtained. Isolated AAVs may be produced using recombinant methods. Such AAVs are referred to herein as "recombinant AAVs". Recombinant AAVs (rAAVs) preferably have tissue-specific targeting capabilities, such that a nuclease and/or transgene of the rAAV will be delivered specifically to one or more predetermined tissue(s). The AAV capsid is an important element in determining these tissue-specific targeting capabilities. Thus, a rAAV having a capsid appropriate for the tissue being targeted can be selected.

Methods for obtaining recombinant AAVs having a desired capsid protein are well known in the art. (See, for example, US 2003/0138772), the contents of which are incorporated herein by reference in their entirety). Typically the methods involve culturing a host cell which contains a nucleic acid sequence encoding an AAV capsid protein; a functional *rep* gene; a recombinant AAV vector composed of, AAV inverted terminal repeats (ITRs) and a transgene; and sufficient helper functions to permit packaging of the recombinant AAV vector into the AAV capsid proteins. In some embodiments, capsid proteins are structural proteins encoded by the cap gene of an AAV. AAVs comprise three capsid proteins, virion proteins 1 to 3 (named VP1, VP2 and VP3), all of which are transcribed from a single cap gene via alternative splicing. In some embodiments, the molecular weights of VP1, VP2 and VP3 are respectively about 87 kDa, about 72 kDa, and about 62 kDa. In some embodiments, upon translation, capsid proteins form a spherical 60-mer protein shell around the viral genome. In some embodiments, the functions of the capsid proteins are to protect the viral genome, deliver the genome and interact with the host. In some aspects, capsid proteins deliver the viral genome to a host in a tissue specific manner.

The present disclosure is based on the findings that exemplary AAV serotype capsid is capable of delivering the transgene *(e.g., mini-PCDH15)* to the ear (*e.g.,* inner hair cells and outer hair cells, spiral ganglion neurons) or the eyes (*e.g.,* photoreceptors). In some embodiments, an AAV capsid protein is of an AAV serotype selected from the group consisting of AAV9.PHP.B, AAV2.7m8, AAV8BP2, exoAAV, Anc80, AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAVrh8, AAV9, AAV10, and AAVrh10. In some embodiments, the capsid protein is AAV2.7m8 or AAV8BP2. AAV2.7m8 is capable of

delivering a transgene targeting cochlear hair cells and supporting cells and the retina. AAV8BP2 shows enhanced transduction rate to the retina (Isgrig et al., AAV2.7m8 is a powerful viral vector for inner ear gene therapy, *Nature Communications* volume 10, Article number: 427 (2019)). In some embodiments, the capsid protein is of AAV serotype 9 (AAV9). In some embodiments, an AAV capsid protein is of a serotype derived from AAV9, for example AAV9.PHP.B. In some embodiments, the AAV capsid protein comprises the sequence at least 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence set forth in SEQ ID NO: 47. In some embodiments, the AAV capsid is an exoAAV. An exoAAV, refers to an exosome-associated AAV. An exoAAV capsid protein can be selected from the group consisting of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAVrh8, AAV9, AAV10, AAVrh10, and AAV.PHP.B. In some examples, the exoAAV is exoAAV1 or exoAAV9. In other embodiments, the AAV capsid protein is Anc80. Anc80 is an in silico predicted ancestor of the widely studied AAV serotypes 1, 2, 8, and 9. Anc80 is a highly potent in vivo gene therapy AAV capsid for targeting liver, muscle, and retina. The present disclosure, at least in part, is based on the capability of AAV9.PHP.B, exoAAV1, or Anc80 to deliver the transgene (*e.g.*, mini-PCDH15) to most of cells in the ear (*e.g.,* inner hair cells, outer hair cells) and cells in the eye (*e.g.,* photoreceptors).

An exemplary acid sequence of AAV9.PHP.B is set forth in SEQ ID NO: 47

MAADGYLPDWLEDNLSEGIREWWALKPGAPQPKANQQHQDNARGLVLPGYKYLGPGNGLDKGE
PVNAADAAALEHDKAYDQQLKAGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQAKKRLL
EPLGLVEEAAKTAPGKKRPVEQSPQEPDSSAGIGKSGAQPAKKRLNFGQTGDTESVPDPQPIG
EPPAAPSGVGSLTMASGGGAPVADNNEGADGVGSSSGNWHCDSQWLGDRVITTSTRTWALPTY
NNHLYKQISNSTSGGSSNDNAYFGYSTPWGYFDFNRFHCHFSPRDWQRLINNNWGFRPKRLNF
KLFNIQVKEVTDNNGVKTIANNLTSTVQVFTDSDYQLPYVLGSAHEGCLPPFPADVFMIPQYG
YLTLNDGSQAVGRSSFYCLEYFPSQMLRTGNNFQFSYEFENVPFHSSYAHSQSLDRLMNPLID
QYLYYLSRTINGSGQNQQTLKFSVAGPSNMAVQGRNYIPGPSYRQQRVSTTVTQNNNSEFAWP
GASSWALNGRNSLMNPGPAMASHKEGEDRFFPLSGSLIFGKQGTGRDNVDADKVMITNEEEIK
TTNPVATESYGQVATNHQSAQTLAVPFKAQAQTGWVQNQGILPGMVWQDRDVYLQGPIWAKIP
HTDGNFHPSPLMGGFGMKHPPPQILIKNTPVPADPPTAFNKDKLNSFITQYSTGQVSVEIEWE
LQKENSKRWNPEIQYTSNYYKSNNVEFAVNTEGVYSEPRPIGTRYLTRNL (SEQ ID NO: 47)

The nucleic acid sequence encoding the AAV9.PHP.B is set forth in SEQ ID NO: 48.

ATGGCTGCCGATGGTTATCTTCCAGATTGGCTCGAGGACAACCTTAGTGAAGGAATTCGCGAG
TGGTGGGCTTTGAAACCTGGAGCCCCTCAACCCAAGGCAAATCAACAACATCAAGACAACGCT
CGAGGTCTTGTGCTTCCGGGTTACAAATACCTTGGACCCGGCAACGGACTCGACAAGGGGGAG

CCGGTCAACGCAGCAGACGCGGCGGCCCTCGAGCACGACAAGGCCTACGACCAGCAGCTCAAG
GCCGGAGACAACCCGTACCTCAAGTACAACCACGCCGACGCCGAGTTCCAGGAGCGGCTCAAA
GAAGATACGTCTTTTGGGGGCAACCTCGGGCGAGCAGTCTTCCAGGCCAAAAAGAGGCTTCTT
GAACCTCTTGGTCTGGTTGAGGAAGCGGCTAAGACGGCTCCTGGAAAGAAGAGGCCTGTAGAG
CAGTCTCCTCAGGAACCGGACTCCTCCGCGGGTATTGGCAAATCGGGTGCACAGCCCGCTAAA
AAGAGACTCAATTTCGGTCAGACTGGCGACACAGAGTCAGTCCCAGACCCTCAACCAATCGGA
GAACCTCCCGCAGCCCCCTCAGGTGTGGGATCTCTTACAATGGCTTCAGGTGGTGGCGCACCA
GTGGCAGACAATAACGAAGGTGCCGATGGAGTGGGTAGTTCCTCGGGAAATTGGCATTGCGAT
TCCCAATGGCTGGGGGACAGAGTCATCACCACCAGCACCCGAACCTGGGCCCTGCCCACCTAC
AACAATCACCTCTACAAGCAAATCTCCAACAGCACATCTGGAGGATCTTCAAATGACAACGCC
TACTTCGGCTACAGCACCCCCTGGGGGTATTTTGACTTCAACAGATTCCACTGCCACTTCTCA
CCACGTGACTGGCAGCGACTCATCAACAACAACTGGGGATTCCGGCCTAAGCGACTCAACTTC
AAGCTCTTCAACATTCAGGTCAAAGAGGTTACGGACAACAATGGAGTCAAGACCATCGCCAAT
AACCTTACCAGCACGGTCCAGGTCTTCACGGACTCAGACTATCAGCTCCCGTACGTGCTCGGG
TCGGCTCACGAGGGCTGCCTCCCGCCGTTCCCAGCGGACGTTTTCATGATTCCTCAGTACGGG
TATCTGACGCTTAATGATGGAAGCCAGGCCGTGGGTCGTTCGTCCTTTTACTGCCTGGAATAT
TTCCCGTCGCAAATGCTAAGAACGGGTAACAACTTCCAGTTCAGCTACGAGTTTGAGAACGTA
CCTTTCCATAGCAGCTACGCTCACAGCCAAAGCCTGGACCGACTAATGAATCCACTCATCGAC
CAATACTTGTACTATCTCTCAAGAACTATTAACGGTTCTGGACAGAATCAACAAACGCTAAAA
TTCAGTGTGGCCGGACCCAGCAACATGGCTGTCCAGGGAAGAAACTACATACCTGGACCCAGC
TACCGACAACAACGTGTCTCAACCACTGTGACTCAAAACAACAACAGCGAATTTGCTTGGCCT
GGAGCTTCTTCTTGGGCTCTCAATGGACGTAATAGCTTGATGAATCCTGGACCTGCTATGGCC
AGCCACAAAGAAGGAGAGGACCGTTTCTTTCCTTTGTCTGGATCTTTAATTTTTGGCAAACAA
GGAACTGGAAGAGACAACGTGGATGCGGACAAAGTCATGATAACCAACGAAGAAGAAATTAAA
ACTACTAACCCGGTAGCAACGGAGTCCTATGGACAAGTGGCCACAAACCACCAGAGTGCCCAA
ACTTTGGCGGTGCCTTTTAAGGCACAGGCGCAGACCGGCTGGGTTCAAAACCAAGGAATACTT
CCGGGTATGGTTTGGCAGGACAGAGATGTGTACCTGCAAGGACCCATTTGGGCCAAAATTCCT
CACACGGACGGCAACTTTCACCCTTCTCCGCTGATGGGAGGGTTTGGAATGAAGCACCCGCCT
CCTCAGATCCTCATCAAAAACACACCTGTACCTGCGGATCCTCCAACGGCCTTCAACAAGGAC
AAGCTGAACTCTTTCATCACCCAGTATTCTACTGGCCAAGTCAGCGTGGAGATCGAGTGGGAG
CTGCAGAAGGAAAACAGCAAGCGCTGGAACCCGGAGATCCAGTACACTTCCAACTATTACAAG
TCTAATAATGTTGAATTTGCTGTTAATACTGAAGGTGTATATAGTGAACCCCGCCCCATTGGC
ACCAGATACCTGACTCGTAATCTGTAA (SEQ ID NO: 48)

The skilled artisan will also realize that conservative amino acid substitutions may be made to provide functionally equivalent variants, or homologs of the capsid proteins. In some aspects the disclosure embraces sequence alterations that result in conservative amino acid substitutions. As used herein, a conservative amino acid substitution refers to an amino acid substitution that does not alter the relative charge or size characteristics of the protein in which the amino acid substitution is made. Variants can be prepared according to methods for altering polypeptide sequence known to one of ordinary skill in the art such as are found in references that compile such methods, *e.g., Molecular Cloning: A Laboratory Manual*, J.

Sambrook, *et al.*, eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, *et al.*, eds., John Wiley & Sons, Inc., New York. Conservative substitutions of amino acids include substitutions made among amino acids within the following groups: (a) M, I, L, V; (b) F, Y, W; (c) K, R, H; (d) A, G; (e) S, T; (f) Q, N; and (g) E, D. Therefore, one can make conservative amino acid substitutions to the amino acid sequence of the proteins and polypeptides disclosed herein.

In some embodiments, the rAAV is a single stranded AAV (ssAAV). An ssAAV, as used herein, refers to a rAAV with the coding sequence and complementary sequence of the transgene expression cassette on separate strands and are packaged in separate viral capsids. In some embodiments, the rAAV is a self-complementary AAV (scAAV). A scAAV, as used herein, refers to an rAAV with both the coding and complementary sequence of the transgene expression cassette are present on each plus-and minus-strand genome. The coding region of a scAAV was designed to form an intra-molecular double-stranded DNA template. Upon infection, rather than waiting for cell mediated synthesis of the second strand, the two complementary halves of scAAV will associate to form one double stranded DNA (dsDNA) unit that is ready for immediate replication and transcription.

In some embodiments, the rAAV as provided herein, is capable of delivering the transgene (*e.g.*, *mini-PCDH15*) to a mammal. In some examples, the mammal can be a human or a non-human mammal, such as a mouse, a rat, or a non-human primate (*e.g.*, cynomolgus monkey).

In some embodiments, the rAAV, as provided herein, is capable of delivering the transgene (*e.g.*, *mini-PCDH15*) to the ear. In some instances, the rAAV as provided herein, is capable of delivering the transgene (*e.g.*, *mini-PCDH15*) to the cells in the inner ear (*e.g.*, cochlea). In other embodiments, the cells can be cells of the eye. In some examples, the cells can be photoreceptors. Non limiting examples of the target cells are outer hair cells (OHC), inner hair cells (IHC), spiral ganglion neurons, stria vascularis, inner sulcus, spiral ligament, or vestibular system, photoreceptor cells, and other cells in the retina to reinstate the normal pattern or Pcdh15 expression within the photoreceptor inner and outer segments (IS), the outer plexiform layer (OPL), the inner nuclei layer (INL), the ganglion cell layer (GCL), the inner plexiform layer (IPL), and the retinal pigment epithelium (RPE).

The components to be cultured in the host cell to package a rAAV vector in an AAV capsid may be provided to the host cell in *trans*. Alternatively, any one or more of the required components (*e.g.*, recombinant AAV vector, rep sequences, cap sequences, and/or helper functions) may be provided by a stable host cell which has been engineered to contain one or more of the required components using methods known to those of skill in the art. Most suitably, such a stable host cell will contain the required component(s) under the control of an inducible promoter. However, the required component(s) may be under the control of a constitutive promoter. Examples of suitable inducible and constitutive promoters are provided herein, in the discussion of regulatory elements suitable for use with the transgene. In still another alternative, a selected stable host cell may contain selected component(s) under the control of a constitutive promoter and other selected component(s) under the control of one or more inducible promoters. For example, a stable host cell may be generated which is derived from 293 cells (which contain E1 helper functions under the control of a constitutive promoter), but which contain the rep and/or cap proteins under the control of inducible promoters. Still other stable host cells may be generated by one of skill in the art.

In some embodiments, the instant disclosure relates to a host cell containing a nucleic acid that comprises a coding sequence encoding a protein (*e.g.*, mini-PCDH15). In some embodiments, the host cell is a mammalian cell (*e.g.*, a human cell), a yeast cell, a bacterial cell, an insect cell, a plant cell, or a fungal cell.

The recombinant AAV vector, rep sequences, cap sequences, and helper functions required for producing the rAAV of the disclosure may be delivered to the packaging host cell using any appropriate genetic element (vector). The selected genetic element may be delivered by any suitable method, including those described herein. The methods used to construct any embodiment of this disclosure are known to those with skill in nucleic acid manipulation and include genetic engineering, recombinant engineering, and synthetic techniques. See, *e.g.*, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Press, Cold Spring Harbor, N.Y. Similarly, methods of generating rAAV virions are well known and the selection of a suitable method is not a limitation on the present disclosure. See, *e.g.*, K. Fisher *et al.*, *J. Virol.*, 70:520-532 (1993) and U.S. Pat. No. 5,478,745.

In some embodiments, recombinant AAVs may be produced using the triple transfection method (described in detail in U.S. Pat. No. 6,001,650). Typically, the

recombinant AAVs are produced by transfecting a host cell with a recombinant AAV vector (comprising a transgene) to be packaged into AAV particles, an AAV helper function vector, and an accessory function vector. An AAV helper function vector encodes the "AAV helper function" sequences (*e.g.*, rep and cap), which function in *trans* for productive AAV replication and encapsidation. Preferably, the AAV helper function vector supports efficient AAV vector production without generating any detectable wild-type AAV virions (*e.g.*, AAV virions containing functional rep and cap genes). Non-limiting examples of vectors suitable for use with the present disclosure include pHLP19, described in U.S. Pat. No. 6,001,650 and pRep6cap6 vector, described in U.S. Pat. No. 6,156,303, the entirety of both incorporated by reference herein. The accessory function vector encodes nucleotide sequences for non-AAV derived viral and/or cellular functions upon which AAV is dependent for replication (*i.e.*, "accessory functions"). The accessory functions include those functions required for AAV replication, including, without limitation, those moieties involved in activation of AAV gene transcription, stage specific AAV mRNA splicing, AAV DNA replication, synthesis of cap expression products, and AAV capsid assembly. Viral-based accessory functions can be derived from any of the known helper viruses, such as adenovirus, herpesvirus (other than herpes simplex virus type-1), and vaccinia virus.

In some aspects, the disclosure provides transfected host cells. The term "transfection" is used to refer to the uptake of foreign DNA by a cell, and a cell has been "transfected" when exogenous DNA has been introduced inside the cell membrane. A number of transfection techniques are generally known in the art. See, *e.g.*, Graham *et al.* (1973) Virology, 52:456, Sambrook *et al.* (1989) Molecular Cloning, a laboratory manual, Cold Spring Harbor Laboratories, New York, Davis *et al.* (1986) Basic Methods in Molecular Biology, Elsevier, and Chu *et al.* (1981) Gene 13:197. Such techniques can be used to introduce one or more exogenous nucleic acids, such as a nucleotide integration vector and other nucleic acid molecules, into suitable host cells.

A "host cell" refers to any cell that harbors, or is capable of harboring, a substance of interest. Often a host cell is a mammalian cell. A host cell may be used as a recipient of an AAV helper construct, an AAV plasmid, an accessory function vector, or other transfer DNA associated with the production of recombinant AAVs. The term includes the progeny of the original cell which has been transfected. Thus, a "host cell" as used herein may refer to a cell

which has been transfected with an exogenous DNA sequence. It is understood that the progeny of a single parental cell may not necessarily be completely identical in morphology or in genomic or total DNA complement as the original parent, due to natural, accidental, or deliberate mutation.

As used herein, the term "cell line" refers to a population of cells capable of continuous or prolonged growth and division *in vitro*. Often, cell lines are clonal populations derived from a single progenitor cell. It is further known in the art that spontaneous or induced changes can occur in karyotype during storage or transfer of such clonal populations. Therefore, cells derived from the cell line referred to may not be precisely identical to the ancestral cells or cultures, and the cell line referred to includes such variants.

As used herein, the terms "recombinant cell" refers to a cell into which an exogenous DNA segment, such as DNA segment that leads to the transcription of a biologically-active polypeptide or production of a biologically active nucleic acid such as an RNA, has been introduced.

As used herein, the term "vector" includes any genetic element, such as a plasmid, phage, transposon, cosmid, chromosome, artificial chromosome, virus, virion, *etc.*, which is capable of replication when associated with the proper control elements and which can transfer gene sequences between cells. Thus, the term includes cloning and expression vehicles, as well as viral vectors. In some embodiments, useful vectors are contemplated to be those vectors in which the nucleic acid segment to be transcribed is positioned under the transcriptional control of a promoter. A "promoter" refers to a DNA sequence recognized by the synthetic machinery of the cell, or introduced synthetic machinery, required to initiate the specific transcription of a gene. The phrases "operatively positioned," "under control" or "under transcriptional control" means that the promoter is in the correct location and orientation in relation to the nucleic acid to control RNA polymerase initiation and expression of the gene. The term "expression vector or construct" means any type of genetic construct containing a nucleic acid in which part or all of the nucleic acid encoding sequence is capable of being transcribed. In some embodiments, expression includes transcription of the nucleic acid, for example, to generate a biologically-active polypeptide product or functional RNA (*e.g.*, guide RNA) from a transcribed gene.

The foregoing methods for packaging recombinant vectors in desired AAV capsids to produce the rAAVs of the disclosure are not meant to be limiting and other suitable methods will be apparent to the skilled artisan.

The present disclosure, provides a rAAV (*e.g.*, scAAV or ssAAV) comprising a vector (*e.g.,* AAV vectors) for expressing a transgene (*e.g., mini-PCDH15*), such vectors include AAV LTRs (*e.g.,* AAV2 LTRs) and a transgene operably linked to a promoter (*e.g.,* chicken beta actin promoter). In addition, the vector can further comprise certain regulatory elements (*e.g.,* enhancers, kozak sequences, and poly adenylation sites). In addition, the rAAV can comprise a capsid protein (*e.g.*, AAV9.PHP.B capsid). Such rAAV can deliver transgenes (*e.g., mini-PCDH15*) to target tissues (*e.g.,* ear or eyes). In some embodiments, such rAAV is capable of delivering transgenes (*e.g., mini-PCDH15*) into specific cells in the target tissue, for example, inner hair cell, out hair cell, or photoreceptors of the eye, *etc.*

III. Pharmaceutical Composition for Delivering Transgenes to the Ear

The rAAVs may be delivered to a subject in compositions according to any appropriate methods known in the art. The rAAV, preferably suspended in a physiologically compatible carrier (*i.e.*, in a composition), may be administered to a subject, *i.e.* host animal. In some embodiments, the host animal is a mammal. In some examples, the mammal is a human. In other embodiments, the mammal can be a non-human mammal, such as a human, mouse, rat, cat, dog, sheep, rabbit, horse, cow, goat, pig, guinea pig, hamster, chicken, turkey, or a non-human primate (*e.g.*, cynomolgus monkey).

Delivery of the rAAVs to a mammalian subject may be by, for example, injection to the ear or the eye. In some embodiments, the injection is to the ear through round window membrane of the inner ear or topical administration (*e.g.*, ear drops). In some embodiments, the injection is the eye (*e.g.,* intravitreal or subretinal injection) or topical administration (*e.g.,* eye drops). In some embodiments, the injection is not topical administration. Combinations of administration methods (*e.g.*, topical administration and injection through round window membrane of the inner ear) can also be used.

The compositions of the disclosure may comprise a rAAV alone, or in combination with one or more other viruses (*e.g.*, a second rAAV encoding having one or more different

transgenes). In some embodiments, a composition comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more different rAAVs each having one or more different transgenes.

In some embodiments, a composition further comprises a pharmaceutically acceptable carrier. Suitable carriers may be readily selected by one of skill in the art in view of the indication for which the rAAV is directed. "Acceptable" means that the carrier must be compatible with the active ingredient of the composition (and preferably, capable of stabilizing the active ingredient) and not deleterious to the subject to be treated. Pharmaceutically acceptable excipients (carriers) including buffers, which are well known in the art. See, *e.g.*, *Remington: The Science and Practice of Pharmacy* 20th Ed. (2000) Lippincott Williams and Wilkins, Ed. K. E. Hoover. For example, one acceptable carrier includes saline, which may be formulated with a variety of buffering solutions (*e.g.*, phosphate buffered saline). Other exemplary carriers include sterile saline, lactose, sucrose, calcium phosphate, gelatin, dextran, agar, pectin, peanut oil, sesame oil, and water. The selection of the carrier is not a limitation of the present disclosure.

The rAAV containing pharmaceutical composition disclosed herein may further comprise a suitable buffer agent. A buffer agent is a weak acid or base used to maintain the pH of a solution near a chosen value after the addition of another acid or base. In some examples, the buffer agent disclosed herein can be a buffer agent capable of maintaining physiological pH despite changes in carbon dioxide concentration (produced by cellular respiration). Exemplary buffer agents include, but are not limited to, HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) buffer, Dulbecco's phosphate-buffered saline (DPBS) buffer, or Phosphate-buffered Saline (PBS) buffer. Such buffers may comprise disodium hydrogen phosphate and sodium chloride, or potassium dihydrogen phosphate and potassium chloride.

Optionally, the compositions of the disclosure may contain, in addition to the rAAV and carrier(s), other pharmaceutical ingredients, such as preservatives, or chemical stabilizers. Suitable exemplary preservatives include chlorobutanol, potassium sorbate, sorbic acid, sulfur dioxide, propyl gallate, the parabens, ethyl vanillin, glycerin, phenol, and parachlorophenol. Suitable chemical stabilizers include gelatin and albumin.

The rAAV containing pharmaceutical composition described herein comprises one or more suitable surface-active agents, such as a surfactant. Surfactants are compounds that lower the surface tension (or interfacial tension) between two liquids, between a gas and a liquid, or

between a liquid and a solid. Surfactants may act as detergents, wetting agents, emulsifiers, foaming agents, and dispersants. Suitable surfactants include, in particular, non-ionic agents, such as polyoxyethylenesorbitans (*e.g.*, TweenTM 20, 40, 60, 80 or 85) and other sorbitans (*e.g.*, SpanTM 20, 40, 60, 80 or 85). Compositions with a surface-active agent will conveniently comprise between 0.05 and 5% surface-active agent, and can be between 0.1 and 2.5%. It will be appreciated that other ingredients may be added, for example mannitol or other pharmaceutically acceptable vehicles, if necessary.

The rAAVs are administered in sufficient amounts to transfect the cells of a desired tissue (*e.g.*, inner hair cells, outer hair cells, or photoreceptors of the eye) and to provide sufficient levels of gene transfer and expression without undue adverse effects. Examples of pharmaceutically acceptable routes of administration include, but are not limited to, direct delivery to the selected organ (*e.g.*, the ear and the eye), oral, inhalation (including intranasal and intratracheal delivery), intraocular, intravenous, intramuscular, subcutaneous, intradermal, intratumoral, and other parental routes of administration. Routes of administration may be combined, if desired.

The dose of rAAV virions required to achieve a particular "therapeutic effect," *e.g.*, the units of dose in viral genome copies/per kilogram of body weight (GC/kg or VG/kg), will vary based on several factors including, but not limited to: the route of rAAV virion administration, the level of gene or RNA expression required to achieve a therapeutic effect, the specific disease or disorder being treated, and the stability of the gene or RNA product. One of skill in the art can readily determine a rAAV virion dose range to treat a patient having a particular disease or disorder based on the aforementioned factors, as well as other factors.

An effective amount of a rAAV is an amount sufficient to target infect an animal (*e.g.*, mouse, rat, non-human primate or human), target a desired tissue (*e.g.*, the inner ear or the eye). The effective amount will depend primarily on factors such as the species, age, weight, health of the subject, and the tissue to be targeted, and may thus vary among animal and tissue. For example, an effective amount of the rAAV is generally in the range of from about 1 ml to about 100 ml of solution containing from about 10^9 to 10^{16} genome copies. In some cases, a dosage between about 10^{11} to 10^{13} rAAV genome copies is appropriate. In certain embodiments, 10^9 rAAV genome copies is effective to target inner ear tissue (*e.g.*, inner hair cells, out hair cells or photoreceptors of the eye). In some embodiments, a dose more

concentrated than 10^9 rAAV genome copies is toxic when administered to the eye of a subject. In some embodiments, an effective amount is produced by multiple doses of a rAAV.

In some embodiments, a dose of rAAV is administered to a subject no more than once per calendar day (*e.g.*, a 24-hour period). In some embodiments, a dose of rAAV is administered to a subject no more than once per 2, 3, 4, 5, 6, or 7 calendar days. In some embodiments, a dose of rAAV is administered to a subject no more than once per calendar week (*e.g.*, 7 calendar days). In some embodiments, a dose of rAAV is administered to a subject no more than bi-weekly (*e.g.*, once in a two calendar week period). In some embodiments, a dose of rAAV is administered to a subject no more than once per calendar month (*e.g.*, once in 30 calendar days). In some embodiments, a dose of rAAV is administered to a subject no more than once per six calendar months. In some embodiments, a dose of rAAV is administered to a subject no more than once per calendar year (*e.g.*, 365 days or 366 days in a leap year).

In some embodiments, rAAV compositions are formulated to reduce aggregation of AAV particles in the composition, particularly where high rAAV concentrations are present (*e.g.*, ~10^{13} GC/ml or more). Appropriate methods for reducing aggregation of may be used, including, for example, addition of surfactants, pH adjustment, salt concentration adjustment, *etc.* (See, *e.g.*, Wright *et al.*, *Molecular Therapy* (2005) 12, 171–178, the contents of which are incorporated herein by reference.)

Formulation of pharmaceutically-acceptable excipients and carrier solutions is well-known to those of skill in the art, as is the development of suitable dosing and treatment regimens for using the particular compositions described herein in a variety of treatment regimens. Typically, these formulations may contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 70% or 80% or more of the weight or volume of the total formulation. Naturally, the amount of active compound in each therapeutically-useful composition may be prepared is such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one skilled in the art of preparing such pharmaceutical formulations, and as such, a variety of dosages and treatment regimens may be desirable.

In some embodiments, rAAVs in suitably formulated pharmaceutical compositions disclosed herein are delivered directly to target tissue, *e.g.*, direct to inner ear tissue (*e.g.*,inner hair cells, outer hair cells or photoreceptors of the eye). In other embodiments, the target tissue can be an eye. The rAAVs in suitably formulated pharmaceutical compositions disclosed herein are delivered directly to the eye (*e.g.,* photoreceptors). However, in certain circumstances it may be desirable to separately or in addition deliver the rAAV-based therapeutic constructs via another route, *e.g.*, subcutaneously, intrapancreatically, intranasally, parenterally, intravenously, intramuscularly, intrathecally, or orally, intraperitoneally, or by inhalation. In some embodiments, the administration modalities as described in U.S. Pat. Nos. 5,543,158; 5,641,515 and 5,399,363 (each specifically incorporated herein by reference in its entirety) may be used to deliver rAAVs.

The pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations contain a preservative to prevent the growth of microorganisms. In many cases the form is sterile and fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (*e.g.*, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. The prevention of the action of microorganisms can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

For administration of an injectable aqueous solution, for example, the solution may be suitably buffered, if necessary, and the liquid diluent first rendered isotonic with sufficient

saline or glucose. These particular aqueous solutions are especially suitable for intravenous administration, intramuscular administration, subcutaneous administration, intraperitoneal administration, subretinal administration, intravitreal administration, and injection through round window membrane of the inner ear. In this connection, a suitable sterile aqueous medium may be employed. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml of hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the host. The person responsible for administration will, in any event, determine the appropriate dose for the individual host.

Sterile injectable solutions are prepared by incorporating the active rAAV in the required amount in the appropriate solvent with various of the other ingredients enumerated herein, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the various sterilized active ingredients into a sterile vehicle which contains the basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum-drying and freeze-drying techniques which yield a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

The rAAV compositions disclosed herein may also be formulated in a neutral or salt form. Pharmaceutically-acceptable salts, include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective. The formulations are easily administered in a variety of dosage forms such as injectable solutions, drug-release capsules, and the like.

As used herein, "carrier" includes any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Supplementary active ingredients can also be incorporated into the compositions. The phrase "pharmaceutically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a host.

Delivery vehicles such as liposomes, nanocapsules, microparticles, microspheres, lipid particles, vesicles, and the like, may be used for the introduction of the compositions of the present disclosure into suitable host cells. In particular, the rAAV vector delivered transgenes may be formulated for delivery either encapsulated in a lipid particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like.

Such formulations may be preferred for the introduction of pharmaceutically acceptable formulations of the nucleic acids or the rAAV constructs disclosed herein. The formation and use of liposomes is generally known to those of skill in the art. Recently, liposomes were developed with improved serum stability and circulation half-times (U.S. Pat. No. 5,741,516). Further, various methods of liposome and liposome like preparations as potential drug carriers have been described (U.S. Pat. Nos. 5,567,434; 5,552,157; 5,565,213; 5,738,868 and 5,795,587).

Liposomes have been used successfully with a number of cell types that are normally resistant to transfection by other procedures. In addition, liposomes are free of the DNA length constraints that are typical of viral-based delivery systems. Liposomes have been used effectively to introduce genes, drugs, radiotherapeutic agents, viruses, transcription factors and allosteric effectors into a variety of cultured cell lines and animals. In addition, several successful clinical trials examining the effectiveness of liposome-mediated drug delivery have been completed.

Liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs). MLVs generally have diameters of from 25 nm to 4 μm. Sonication of MLVs results in the formation of small unilamellar vesicles (SUVs) with diameters in the range of 200 to 500 Å, containing an aqueous solution in the core.

Alternatively, nanocapsule formulations of the rAAV may be used. Nanocapsules can generally entrap substances in a stable and reproducible way. To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1 μm) should be designed using polymers able to be degraded *in vivo*. Biodegradable polyalkyl-cyanoacrylate nanoparticles that meet these requirements are contemplated for use.

IV. Therapeutic Applications

The present disclosure also provides methods for delivering a transgene (*e.g.*, mini-PCDH15) to the ear or the eye for treating hearing loss and/or blindness (*e.g.*, Usher Syndrome type 1F).

In some embodiments, the subject can be a mammal. In some examples, the subject can be a human. In other embodiments, the subject can be a non-human mammal such as mouse, rat, cow, goat, pig, camel, and non-human primate (*e.g.*, cynomolgus monkey).

In some embodiments, the subject is having or suspected of having hearing loss and/or blindness. In some examples, the subject is diagnosed of having Usher Syndrome type 1F. In further examples, the hearing loss and/or blindness is associated with a mutation in the PCDH15 gene. In some examples, the mutation of PCDH15 gene is a point mutation, a missense mutation, a nonsense mutation, a deletion, an insertion or a combination thereof. Non-limiting exemplary mutations in PCDH15 are shown in Table 1. A mutation, as used herein, refers to a substitution of a residue within a sequence, *e.g.*, a nucleic acid or amino acid sequence, with another residue, or a deletion or insertion of one or more residues within a sequence. Mutations are typically described herein by identifying the original residue followed by the position of the residue within the sequence and by the identity of the newly substituted residue. Various methods for making the amino acid substitutions (mutations) provided herein are well known in the art, and are provided by, for example, Green and Sambrook, Molecular Cloning: A Laboratory Manual (4th ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (2012)).

Table 1: Exemplary mutations in PCDH15

Accession NO:	Mutation	Amino Acid Change
NM_033056.3(PCDH15)	c.400C>G	p.Arg134Gly

NM_033056.3(PCDH15)	c.733C>T	p.Arg245Ter
NM_033056.3(PCDH15)	c.785G>A	p.Gly262Asp
NM_033056.3(PCDH15)	c.1583T>A	p.Val528Asp
NM_033056.3(PCDH15)	c.3316C>T	p.Arg1106Ter
NM_001142769.2(PCDH15)	c.4726C>T	p.Gln1576Ter
NM_033056.3(PCDH15)	c.4035T>A	p.Tyr1345Ter
NM_033056.3(PCDH15)	c.1997+1G>A	
NM_033056.3(PCDH15)	c.3984-1G>C	
	GRCh38/hg38 10q21.1(chr10:53954459-54098171)x0	
NM_033056.3(PCDH15)	c.158-1G>A	
NM_033056.3(PCDH15)	c.16delT	p.Tyr6Ilefs
NM_001142763.1(PCDH15)	c.2986C>T	p.Arg996Ter
NM_033056.3(PCDH15)	c.1998-2A>G	
NM_033056.3(PCDH15)	c.1927C>T	p.Arg643Ter
NM_033056.3(PCDH15)	c.3358C>T ()	p.Arg1120Ter
PCDH15, IVS27, A-G, -2		
NM_033056.3(PCDH15)	c.(?_-15)_(876_?)	del
NM_033056.3(PCDH15)	c.706-3_717delCAGGACCGTGCCCAA	
NM_033056.3(PCDH15)	c.(?_3374)_(3501_?)	del (p.(?))
NM_033056.3(PCDH15)	c.1940C>G	p.Ser647Ter
NM_033056.3(PCDH15)	c.1086delT	p.Leu363Trpfs

NM_001142772.1(PCDH15)	c.400C>T	p.Arg134Ter
NM_033056.3(PCDH15)	c.2419dupA	p.Ile807Asnfs
NM_033056.3(PCDH15)	c.7C>T	p.Arg3Ter
PCDH15,	3-BP DEL, 5601AAC	
NM_033056.3(PCDH15)	c.394dupG	p.Glu132Glyfs
PCDH15,	1-BP DEL, 16T	
NM_001142763.1(PCDH15)	c.(?_-1)_(2235+1_2236-1)	del
NM_001142763.1(PCDH15)	c.5385_5394delTCCTCTTCCT	p.Pro1796Leufs
NC_000010.10	g.56104359_56108448del4090	
NC_000010.10	g.55829578_56723036del893459	
NM_033056.3(PCDH15)	c.157+1G>C	
NM_033056.3(PCDH15)	c.3885_3889dup	p.Ala1297Glufs
NM_033056.3(PCDH15)	c.2825delG	p.Gly942Valfs
NM_033056.3(PCDH15)	c.3983+1G>T	
NM_033056.3(PCDH15)	c.1770_1771delTC	p.Pro591Cysfs
NM_001142763.1	c.-189197_c.610-5166del	
NM_033056.3(PCDH15)	c.416_444del29 ()	p.Asp139Alafs
NM_033056.3(PCDH15)	c.3653delT	p.Phe1218Serfs
NM_033056.3(PCDH15)	c.3717+1G>A	

NM_033056.3(PCDH15)	c.2624C>A	p.Ser875Ter
NM_033056.3(PCDH15)	c.2785C>T ()	p.Arg929Ter
NM_033056.3(PCDH15)	c.4313delC ()	p.Pro1438Argfs
NM_033056.3(PCDH15)	c.2487dupA ()	p.Glu830Argfs
NM_033056.3(PCDH15)	c.4368-2A>T	
NM_033056.3(PCDH15)	c.4368-15_4368-2delTTCTTTTCTTTCAA	
NM_033056.3(PCDH15)	c.1785-2A>C	
NM_033056.3(PCDH15)	c.4227T>A ()	p.Cys1409Ter
NM_033056.3(PCDH15)	c.594+1G>T	
NM_033056.3(PCDH15)	c.1006C>T ()	p.Arg336Ter
NM_033056.3(PCDH15)	c.1305+1G>A	
NM_033056.3(PCDH15)	c.901dupA	p.Thr301Asnfs
NM_033056.3(PCDH15)	c.3211delA	p.Ile1071Leufs
NM_033056.3(PCDH15)	c.333dupA	p.His112Thrfs
NM_033056.3(PCDH15)	c.3341delT	p.Val1114Glyfs
NM_033056.3(PCDH15)	c.4367+1G>A	
NM_033056.3(PCDH15)	c.1627delG	p.Glu543Argfs
NM_033056.3(PCDH15)	c.4197_4198insGTAG	p.Arg1400Valfs
NM_033056.3(PCDH15)	c.4211+2dupT	

NM_033056.3(PCDH15)	c.1806T>G	p.Tyr602Ter
NM_033056.3(PCDH15)	c.3441dupA	p.Phe1148Ilefs
NM_033056.3(PCDH15)	c.3082delC	p.His1028Ilefs
NM_033056.3(PCDH15)	c.1830_1833delTCAA	p.Asn610Lysfs
NM_033056.3(PCDH15)	c.1737C>G	p.Tyr579Ter
NM_033056.3(PCDH15)	c.358_359delTG	p.Cys120Hisfs
NM_033056.3(PCDH15)	c.3023delC	p.Ala1008Valfs
NM_033056.3(PCDH15)	c.1915C>T	p.Gln639Ter
NM_033056.3(PCDH15)	c.*12348A>G	
NM_033056.3(PCDH15)	c.5435C>T	p.Pro1812Leu
NM_001142771.1(PCDH15)	c.4627G>A	p.Gly1543Ser
NM_033056.3(PCDH15)	c.2367_2369delTGT	p.Val790del
NM_033056.3(PCDH15)	c.1362C>T	p.Val454=
NM_033056.3(PCDH15)	c.3502-8C>T	
NM_033056.3(PCDH15)	c.330C>T	p.Asn110=
NM_033056.3(PCDH15)	c.5601_5603delAAC	p.Thr1869del
NM_033056.3(PCDH15)	c.5280_5342del63	p.Ala1761_Pro1781del
NM_033056.3(PCDH15)	c.243G>A	p.Val81=

NM_033056.3(PCDH15)	c.5287_5292delGCTCCT	p.Ala1763_Pro1764del
NM_033056.3(PCDH15)	c.2885G>T	p.Arg962Leu
NM_033056.3(PCDH15)	c.2424G>C	p.Lys808Asn
NM_033056.3(PCDH15)	c.3195A>G	p.Gln1065=
NM_033056.3(PCDH15)	c.4812G>T ()	p.Arg1604Ser
NM_033056.3(PCDH15)	c.5353T>C ()	p.Ser1785Pro
NM_033056.3(PCDH15)	c.5283T>A	p.Ala1761=
NM_033056.3(PCDH15)	c.4783A>C	p.Ile1595Leu
NM_033056.3(PCDH15)	c.475-3C>T	
NM_033056.3(PCDH15)	c.4334C>G	p.Ala1445Gly
NM_033056.3(PCDH15)	c.2884C>T	p.Arg962Cys
NM_033056.3(PCDH15)	c.3983+12T>C	
NM_033056.3(PCDH15)	c.960A>G	p.Pro320=
NM_033056.3(PCDH15)	c.546A>G	p.Gly182=
NM_033056.3(PCDH15)	c.1910A>G	p.Asn637Ser
NM_033056.3(PCDH15)	c.2625G>A	p.Ser875=
NM_033056.3(PCDH15)	c.5359C>T	p.Pro1787Ser
NM_001142763.1(PCDH15)	c.4871A>G	p.Asn1624Ser
NM_033056.3(PCDH15)	c.2563C>T	p.Arg855Trp

NM_033056.3(PCDH15)	c.5254_5256delCCT	p.Pro1752del
NM_033056.3(PCDH15)	c.3018G>T	p.Val1006=
NM_033056.3(PCDH15)	c.4831_4834dupAACA	p.Thr1612Lysfs
NM_033056.3(PCDH15)	c.5565C>T	p.Ala1855=
NM_033056.3(PCDH15)	c.3795A>T	p.Glu1265Asp
NM_033056.3(PCDH15)	c.4080G>A	p.Val1360=
NM_033056.3(PCDH15)	c.1360G>A	p.Val454Ile
NM_033056.3(PCDH15)	c.3936A>G	p.Ala1312=

Aspects of the present disclosure relates to method of treating hearing loss and/or blindness (*e.g.,* Usher Syndrome type 1F) by delivering a functional gene product (*e.g.*, mini-PCDH15) using gene therapy (*e.g.,* rAAV encoding mini-PCDH15) to a target cells (*e.g.,* inner hair cell, outer hair cell, and photoreceptors), which comprise one or more mutations in both alleles in a relevant gene (*e.g., PCDH15*) that results in absence or malfunction of the gene product.

Other aspects of the present disclosure relates to method of treating hearing loss and/or blindness (*e.g.,* Usher Syndrome type 1F) by correcting one or more mutations (*e.g.,* point mutations) in a relevant gene (*e.g., PCDH15*) in a target cell (*e.g.,* inner hair cell, outer hair cell, and photoreceptors) using base editors (*e.g.,* ABEmax). Non-limiting exemplary mutations can be found in Table 1.

(i) Methods for Delivering Functional mini-PCDH15

Aspects of the invention relate to certain protein-encoding transgenes (*e.g.*, *mini-PCDH15*) that when delivered to a subject an effective for promoting cell adhesion the inner ear and in the retina of the subject. In some embodiments, the subject has or is suspected of

having hearing loss and/or blindness. In some examples, the hearing loss and/or blindness is associated with a mutation of the *PCDH15* gene. In one example, the subject is diagnosed with Usher Syndrome, type 1F.

Accordingly, methods and compositions described by the disclosure are useful, in some embodiments, for the treatment of Usher syndrome, Type 1F associated with one or more mutations or deletions of *PCDH15* gene, such as hearing loss, deafness, and/or progressive vision loss, and blindness.

Methods for delivering a transgene (*e.g.*, mini-*PCDH15*) to a subject are provided by the disclosure. The methods typically involve administering to a subject an effective amount of an isolated nucleic acid encoding a mini-PCDH15, or a rAAV comprising a nucleic acid for expressing a mini-PCDH15.

In some embodiments, the hearing loss and/or blindness is Usher syndrome type 1F. Generally, a mutation or mutations in *PCDH15* account for Usher syndrome type 1F. In some embodiments, the *PCDH15* mutation can be, but are not limited to, point mutations, missense mutations, nonsense mutations, insertions, or deletions. In some examples, the *PCDH15* gene mutations associated with Usher syndrome, type 1F include but are not limited to mutations in Table 1 (ClinVar, NCBI). In one example, the mutation in PCDH15 is c.733C>T. Mutations in a *PCDH15* gene of a subject (*e.g.*, a subject having or suspected of having Usher Syndrome type 1F associated with a deletion or mutation of *PCDH15* gene) may be identified from a sample obtained from the subject (*e.g.*, a DNA sample, RNA sample, blood sample, or other biological sample) by any method known in the art. For example, in some embodiments, a nucleic acid (*e.g.*, DNA, RNA, or a combination thereof) is extracted from a biological samples obtained from a subject and nucleic acid sequencing is performed in order to identify a mutation in the *PCDH15* gene. Examples of nucleic acids sequencing techniques include but are not limited to Maxam-Gilbert sequencing, pyrosequencing, chain-termination sequencing, massively parallel signature sequencing, single-molecule sequencing, nanopore sequencing, Illumina sequencing, *etc.* In some embodiments, a mutation in *PCDH15* gene is detected indirectly, for example by quantifying mini-PCDH15 protein expression (*e.g.*, by Western blot) or function (*e.g.*, by analyzing structure, function, *etc.*), or by direct sequencing of the DNA and comparing the sequence obtained to a control DNA sequence (*e.g.*, a wild-type *PCDH15* DNA sequence).

In some aspects, the disclosure provides a method for treating an Usher syndrome type 1F in a subject in need thereof, the method comprising administering to a subject having or is suspected of having Usher syndrome type 1F a therapeutically effective amount of an isolated nucleic acid, or a rAAV encoding a transgene (*e.g., mini-PCDH15*) through injections to the round window membrane of the inner ear, as described by the disclosure. In other embodiments, the injection is to the eye (*e.g.,* intravitreal injection)

An "effective amount" of a substance is an amount sufficient to produce a desired effect. In some embodiments, an effective amount of an isolated nucleic acid (*e.g.*, an isolated nucleic acid comprising a transgene encoding mini-PCDH15) is an amount sufficient to transfect (or infect in the context of rAAV mediated delivery) a sufficient number of target cells of a target tissue of a subject. In some embodiments, a target tissue is cochlear (*e.g.*, inner hair cells, outer hair cells, *etc.*). In other embodiments, a target tissue is the eye (*e.g.*, photoreceptors). In some embodiments, an effective amount of an isolated nucleic acid (*e.g.*, which may be delivered via an rAAV) may be an amount sufficient to have a therapeutic benefit in a subject, *e.g.*, to increase or supplement the expression of a gene or protein of interest (*e.g.*, mini-PCDH15), to improve in the subject one or more symptoms of disease (*e.g.*, a symptom of Usher syndrome type 1F), *etc.* The effective amount will depend on a variety of factors such as, for example, the species, age, weight, health of the subject, and the tissue to be targeted, and may thus vary among subject and tissue as described elsewhere in the disclosure.

In some embodiments, the method is for delivering a transgene to cochlear (*e.g.*, inner hair cells, and outer hair cells) tissue in a subject are provided herein. In other embodiments, the method is for delivering a transgene to the cells in the eye (*e.g.,* photoreceptors). The methods typically involve administering to a subject an effective amount of a rAAV comprising a nucleic acid for expressing a transgene (*e.g.*, *mini-PCDH15*) in the subject. An "effective amount" of a rAAV is an amount sufficient to infect a sufficient number of cells of a target tissue in a subject. In some embodiments, a target tissue is cochlea (*e.g.*, inner hair cells, outer hair cells) tissue. In other embodiments, the target tissue is the retina (*e.g.,* photoreceptors). An effective amount of a rAAV may be an amount sufficient to have a therapeutic benefit in a subject, *e.g.*, to improve in the subject one or more symptoms of disease, *e.g.*, a symptom of a hereditary hearing loss (*e.g.*, Usher syndrome type 1F). In some cases, an effective amount of a rAAV may be an amount sufficient to produce a stable somatic

transgenic animal model. The effective amount will depend on a variety of factors such as, for example, the species, age, weight, health of the subject, and the tissue to be targeted, and may thus vary among subject and tissue.

An effective amount may also depend on the rAAV used. The invention is based, in part on the recognition that rAAV comprising capsid proteins having a particular serotype (*e.g.,* AAV9.PHP.B, exoAAV, and Anc80) mediate more efficient transduction of cochlear (*e.g.*, inner hair cells, out hair cells) tissue that rAAV comprising capsid proteins having a different serotype.

In certain embodiments, the effective amount of rAAV is 10^{10}, 10^{11}, 10^{12}, 10^{13}, or 10^{14} genome copies per kg. In certain embodiments, the effective amount of rAAV is 10^{10}, 10^{11}, 10^{12}, 10^{13}, 10^{14}, or 10^{15} genome copies per subject.

An effective amount may also depend on the mode of administration. For example, targeting a cochlear (*e.g.*, inner hair cells, and out hair cells) tissue by injection through the round window membrane of the inner ear may require different (*e.g.*, higher or lower) doses, in some cases, than targeting a cochlea (*e.g.*, inner hair cells, out hair cells) tissue by another method (*e.g.*, systemic administration, topical administration). In other cases, targeting the eye (*e.g.,* photoreceptors) by injection behind the eye (*e.g.,* subretinal injection and intravitreal injection) may require different does, in some cases, than targeting the eye (*e.g.,* photoreceptors) by another method (*e.g.*, systemic administration, topical administration). Thus, in some embodiments, the injection is injection through round window membrane of the inner ear. In some embodiments, the administration is via injection, optionally subretinal injection or intravitreal injection. In some embodiments, the injection is topical administration (*e.g.*, topical administration to an ear) , or posterior semicircular canal injection. In some cases, multiple doses of a rAAV are administered.

Without wishing to be bound by any particular theory, efficient transduction of cochlear (*e.g.*, inner hair cells, out hair cells, or photoreceptors) cells by rAAV described herein may be useful for the treatment of a subject having a hereditary hearing loss and/or vision loss (*e.g.*, Usher syndrome type 1F). Accordingly, methods and compositions for treating hereditary hearing loss are also provided herein. In some aspects, the disclosure provides a method for treating a hereditary hearing loss and or vision loss (*e.g.*, Usher syndrome type 1F), the method comprising: administering to a subject having or suspected of

having an a hereditary hearing loss an effective amount of rAAV, wherein the rAAV comprises (i) a capsid protein having a serotype of AAV9.PHP.B, exoAAV1 or Anc80, and (ii) an isolated nucleic acid comprising a promoter operably linked to a transgene (*e.g.*, a transgene encoding a mini-PCDH15) and AAV LTRs.

In some embodiments, the rAAV (e.g., rAAV encoding mini-PCDH15) can be administered to the patients (e.g., patients with Usher 1F syndrome or hereditary hearing loss) at age of 6 month, 1 year, 2 years, 3 years, 5 years, 6 years, 7 years, 8 years, 9, years, 10 years, 11 years, 12 years, 13 years, 14 years, 15 years, 16 years, 17 years, 18 years or older. In some embodiments, the patient is an infant, a child, or an adult. In some embodiments, the rAAV (e.g., rAAV encoding mini-PCDH15) can be administered to the patients (e.g., patients with Usher 1F syndrome or hereditary hearing loss) once in a life time, every 5 years, every 2 years, every year, every 6 months, every 3 months, every month, every two weeks, every week. In other embodiments, the administration of the rAAV (e.g., rAAV encoding mini-PCDH15) can be administered to the patients (e.g., patients with Usher 1F syndrome or hereditary hearing loss) in combination with other known treatment methods for Usher 1F or hereditary hearing (e.g., Vitamin A supplementation).

(ii) Methods for Correcting Mutations in PCDH15 Gene Using Base Editors

Other aspects of the present disclosure relates to method of treating hearing loss and/or blindness (*e.g.,* Usher Syndrome type 1F) by correcting one or more mutations (*e.g.,* point mutations) in a relevant gene (*e.g., PCDH15*) in a target cell (*e.g.,* inner hair cell, outer hair cell, and photoreceptors) using base editors (*e.g.,* ABEmax). Non-limiting exemplary mutations can be found in table 1.

In some embodiments, the method for correcting a point mutation of PCDH15 on a target sequence comprises contacting the target sequence with a base editor and a guide RNA. A target sequence, as used herein, refers to a sequence within a nucleic acid molecule that is deaminated by a deaminase or a fusion protein comprising a deaminase, (*e.g.*, a dCas9-adenosine deaminase fusion protein). The present disclosure provides methods of using the base editor, or complexes comprising a guide nucleic acid (*e.g.*, gRNA) and a nucleobase editor provided herein. For example, some aspects of this disclosure provide methods comprising contacting a DNA molecule with any of the fusion proteins provided herein, and

with at least one guide nucleic acid (*e.g.*, guide RNA), wherein the guide nucleic acid, (*e.g.*, guide RNA) is about 15-100 nucleotides long and comprises a sequence of at least 10 contiguous nucleotides that is complementary to a target sequence.

In some embodiments, the target DNA sequence comprises a G>A or C>T (*e.g.*, c.733C>T mutation on the coding strand of *PCDH15* results in a G>A point mutation on the complementary strand) point mutation associated with a disease or disorder, and wherein the deamination of the mutant A base results in a sequence that is not associated with a disease or disorder. In some embodiments, the target DNA sequence encodes a protein, and the point mutation is in a codon and results in a change in the amino acid encoded by the mutant codon as compared to the wild-type codon. In some embodiments, the deamination of the mutant A results in a change of the amino acid encoded by the mutant codon. In some embodiments, the deamination of the mutant A results in the codon encoding the wild-type amino acid. In some embodiments, the target sequence can is in the genome of a subject. In some examples, the subject is a mammal. In one example, the subject is a human. In other examples, the subject is a non-human mammal, such as mouse, rat, cat, dog, sheep, rabbit, horse, cow, goat, pig, guinea pig, hamster, chicken, turkey, or a non-human primate (*e.g.*, cynomolgus monkey).

A base editor (BE)," or "nucleobase editor (NBE)", as used herein, refers to an agent comprising a polypeptide that is capable of making a modification to a base (*e.g.*, A, T, C, G, or U) within a nucleic acid sequence (*e.g.*, DNA or RNA). In some embodiments, the base editor is capable of deaminating a base within a nucleic acid. In some embodiments, the base editor is capable of deaminating a base within a DNA molecule. In some embodiments, the base editor is capable of deaminating an adenine (A) in DNA. In some embodiments, the base editor is a fusion protein comprising a nucleic acid programmable DNA binding protein (napDNAbp) fused to an adenosine deaminase. In some embodiments, the base editor is a Cas9 protein fused to an adenosine deaminase. In some embodiments, the base editor is a Cas9 nickase (nCas9) fused to an adenosine deaminase. In some embodiments, the base editor is a nuclease-inactive Cas9 (dCas9) fused to an adenosine deaminase. In some embodiments, the base editor is ABEmax. In some embodiments, the base editor is ABE_7. In some embodiments, the base editor is ABE_8. In some embodiments, the base editor is ABE_7. In some embodiments, the base editor is ABE_VRQR. In some embodiments, any of the base

editors described herein can be fused with a Cas9 protein (e.g., Cas9 (D10A) or Cas9 (N)) with or without a linker.

An exemplary amino acid sequence for ABEmax-Cas9 (D10A) is set forth in SEQ ID NO: 157:

MKRTADGSEFESPKKKRKVSEVEFSHEYWMRHALTLAKRAWDEREVPVGAVLVHNNRVIGEGW
NRPIGRHDPTAHAEIMALRQGGLVMQNYRLIDATLYVTLEPCVMCAGAMIHSRIGRVVFGARD
AKTGAAGSLMDVLHHPGMNHRVEITEGILADECAALLSDFFRMRRQEIKAQKKAQSSTDSGGS
SGGSSGSETPGTSESATPESSGGSSGGSSEVEFSHEYWMRHALTLAKRARDEREVPVGAVLVL
NNRVIGEGWNRAIGLHDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRI
GRVVFGVRNAKTGAAGSLMDVLHYPGMNHRVEITEGILADECAALLCYFFRMPRQVFNAQKKA
QSSTDSGGSSGGSSGSETPGTSESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAVITDEYKV
PSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIFSNEM
AKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRL
IYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPINASGVDAKAILSARL
SKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLL
AQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQ
LPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTF
DNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILTFRIPYYVGPLARGNSRFAWMTRK
SEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVT
EGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTY
HDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYT
GWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQVSGQGDSL
HEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRERMKR
IEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRLSDYDVDHIVPQSF
LKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLS
ELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQF
YKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKATAK
YFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDFATVRKVLSMPQVNIVKKT
EVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVK
ELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQKGN
ELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVILADANL
DKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTIDRKRYTSTKEVLDATLIHQ
SITGLYETRIDLSQLGGD

An exemplary nucleic acid sequence encoding ABEmax-Cas9 (D10A) is set forth in SEQ ID NO: 158:

ATGAAACGGACAGCCGACGGAAGCGAGTTCGAGTCACCAAAGAAGAAGCGGAAAGTCTCTGAA
GTCGAGTTTAGCCACGAGTATTGGATGAGGCACGCACTGACCCTGGCAAAGCGAGCATGGGAT
GAAAGAGAAGTCCCCGTGGGCGCCGTGCTGGTGCACAACAATAGAGTGATCGGAGAGGGATGG
AACAGGCCAATCGGCCGCCACGACCCTACCGCACACGCAGAGATCATGGCACTGAGGCAGGGA
GGCCTGGTCATGCAGAATTACCGCCTGATCGATGCCACCCTGTATGTGACACTGGAGCCATGC
GTGATGTGCGCAGGAGCAATGATCCACAGCAGGATCGGAAGAGTGGTGTTCGGAGCACGGGAC
GCCAAGACCGGCGCAGCAGGCTCCCTGATGGATGTGCTGCACCACCCCGGCATGAACCACCGG
GTGGAGATCACAGAGGGAATCCTGGCAGACGAGTGCGCCGCCCTGCTGAGCGATTTCTTTAGA

ATGCGGAGACAGGAGATCAAGGCCCAGAAGAAGGCACAGAGCTCCACCGACTCTGGAGGATCT
AGCGGAGGATCCTCTGGAAGCGAGACACCAGGCACAAGCGAGTCCGCCACACCAGAGAGCTCC
GGCGGCTCCTCCGGAGGATCCTCTGAGGTGGAGTTTTCCCACGAGTACTGGATGAGACATGCC
CTGACCCTGGCCAAGAGGGCACGCGATGAGAGGGAGGTGCCTGTGGGAGCCGTGCTGGTGCTG
AACAATAGAGTGATCGGCGAGGGCTGGAACAGAGCCATCGGCCTGCACGACCCAACAGCCCAT
GCCGAAATTATGGCCCTGAGACAGGGCGGCCTGGTCATGCAGAACTACAGACTGATTGACGCC
ACCCTGTACGTGACATTCGAGCCTTGCGTGATGTGCGCCGGCGCCATGATCCACTCTAGGATC
GGCCGCGTGGTGTTTGGCGTGAGGAACGCAAAAACCGGCGCCGCAGGCTCCCTGATGGACGTG
CTGCACTACCCCGGCATGAATCACCGCGTCGAAATTACCGAGGGAATCCTGGCAGATGAATGT
GCCGCCCTGCTGTGCTATTTCTTTCGGATGCCTAGACAGGTGTTCAATGCTCAGAAGAAGGCC
CAGAGCTCCACCGACTCCGGAGGATCTAGCGGAGGCTCCTCTGGCTCTGAGACACCTGGCACA
AGCGAGAGCGCAACACCTGAAAGCAGCGGGGGCAGCAGCGGGGGGTCAGACAAGAAGTACAGC
ATCGGCCTGGCCATCGGCACCAACTCTGTGGGCTGGGCCGTGATCACCGACGAGTACAAGGTG
CCCAGCAAGAAATTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATC
GGAGCCCTGCTGTTCGACAGCGGCGAAACAGCCGAGGCCACCCGGCTGAAGAGAACCGCCAGA
AGAAGATACACCAGACGGAAGAACCGGATCTGCTATCTGCAAGAGATCTTCAGCAACGAGATG
GCCAAGGTGGACGACAGCTTCTTCCACAGACTGGAAGAGTCCTTCCTGGTGGAAGAGGATAAG
AAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTAC
CCCACCATCTACCACCTGAGAAAGAAACTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTG
ATCTATCTGGCCCTGGCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTG
AACCCCGACAACAGCGACGTGGACAAGCTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTG
TTCGAGGAAAACCCCATCAACGCCAGCGGCGTGGACGCCAAGGCCATCCTGTCTGCCAGACTG
AGCAAGAGCAGACGGCTGGAAAATCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAATGGCCTG
TTCGGAAACCTGATTGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTG
GCCGAGGATGCCAAACTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTG
GCCCAGATCGGCGACCAGTACGCCGACCTGTTTCTGGCCGCCAAGAACCTGTCCGACGCCATC
CTGCTGAGCGACATCCTGAGAGTGAACACCGAGATCACCAAGGCCCCCCTGAGCGCCTCTATG
ATCAAGAGATACGACGAGCACCACCAGGACCTGACCCTGCTGAAAGCTCTCGTGCGGCAGCAG
CTGCCTGAGAAGTACAAAGAGATTTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATT
GACGGCGGAGCCAGCCAGGAAGAGTTCTACAAGTTCATCAAGCCCATCCTGGAAAAGATGGAC
GGCACCGAGGAACTGCTCGTGAAGCTGAACAGAGAGGACCTGCTGCGGAAGCAGCGGACCTTC
GACAACGGCAGCATCCCCCACCAGATCCACCTGGGAGAGCTGCACGCCATTCTGCGGCGGCAG
GAAGATTTTTACCCATTCCTGAAGGACAACCGGGAAAAGATCGAGAAGATCCTGACCTTCCGC
ATCCCCTACTACGTGGGCCCTCTGGCCAGGGGAAACAGCAGATTCGCCTGGATGACCAGAAAG
AGCGAGGAAACCATCACCCCCTGGAACTTCGAGGAAGTGGTGGACAAGGGCGCTTCCGCCCAG
AGCTTCATCGAGCGGATGACCAACTTCGATAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAG
CACAGCCTGCTGTACGAGTACTTCACCGTGTATAACGAGCTGACCAAAGTGAAATACGTGACC
GAGGGAATGAGAAAGCCCGCCTTCCTGAGCGGCGAGCAGAAAAAGGCCATCGTGGACCTGCTG
TTCAAGACCAACCGGAAAGTGACCGTGAAGCAGCTGAAAGAGGACTACTTCAAGAAAATCGAG
TGCTTCGACTCCGTGGAAATCTCCGGCGTGGAAGATCGGTTCAACGCCTCCCTGGGCACATAC
CACGATCTGCTGAAAATTATCAAGGACAAGGACTTCCTGGACAATGAGGAAAACGAGGACATT
CTGGAAGATATCGTGCTGACCCTGACACTGTTTGAGGACAGAGAGATGATCGAGGAACGGCTG
AAAACCTATGCCCACCTGTTCGACGACAAAGTGATGAAGCAGCTGAAGCGGCGGAGATACACC
GGCTGGGGCAGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACA
ATCCTGGATTTCCTGAAGTCCGACGGCTTCGCCAACAGAAACTTCATGCAGCTGATCCACGAC
GACAGCCTGACCTTTAAAGAGGACATCCAGAAAGCCCAGGTGTCCGGCCAGGGCGATAGCCTG
CACGAGCACATTGCCAATCTGGCCGGCAGCCCCGCCATTAAGAAGGGCATCCTGCAGACAGTG

AAGGTGGTGGACGAGCTCGTGAAAGTGATGGGCCGGCACAAGCCCGAGAACATCGTGATCGAA
ATGGCCAGAGAGAACCAGACCACCCAGAAGGGACAGAAGAACAGCCGCGAGAGAATGAAGCGG
ATCGAAGAGGGCATCAAAGAGCTGGGCAGCCAGATCCTGAAAGAACACCCCGTGGAAAACACC
CAGCTGCAGAACGAGAAGCTGTACCTGTACTACCTGCAGAATGGGCGGGATATGTACGTGGAC
CAGGAACTGGACATCAACCGGCTGTCCGACTACGATGTGGACCATATCGTGCCTCAGAGCTTT
CTGAAGGACGACTCCATCGACAACAAGGTGCTGACCAGAAGCGACAAGAACCGGGGCAAGAGC
GACAACGTGCCCTCCGAAGAGGTCGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAAC
GCCAAGCTGATTACCCAGAGAAAGTTCGACAATCTGACCAAGGCCGAGAGAGGCGGCCTGAGC
GAACTGGATAAGGCCGGCTTCATCAAGAGACAGCTGGTGGAAACCCGGCAGATCACAAAGCAC
GTGGCACAGATCCTGGACTCCCGGATGAACACTAAGTACGACGAGAATGACAAGCTGATCCGG
GAAGTGAAAGTGATCACCCTGAAGTCCAAGCTGGTGTCCGATTTCCGGAAGGATTTCCAGTTT
TACAAAGTGCGCGAGATCAACAACTACCACCACGCCCACGACGCCTACCTGAACGCCGTCGTG
GGAACCGCCCTGATCAAAAAGTACCCTAAGCTGGAAAGCGAGTTCGTGTACGGCGACTACAAG
GTGTACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAAATCGGCAAGGCTACCGCCAAG
TACTTCTTCTACAGCAACATCATGAACTTTTTCAAGACCGAGATTACCCTGGCCAACGGCGAG
ATCCGGAAGCGGCCTCTGATCGAGACAAACGGCGAAACCGGGGAGATCGTGTGGGATAAGGGC
CGGGATTTTGCCACCGTGCGGAAAGTGCTGAGCATGCCCCAAGTGAATATCGTGAAAAAGACC
GAGGTGCAGACAGGCGGCTTCAGCAAAGAGTCTATCCTGCCCAAGAGGAACAGCGATAAGCTG
ATCGCCAGAAAGAAGGACTGGGACCCTAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCC
TATTCTGTGCTGGTGGTGGCCAAAGTGGAAAAGGGCAAGTCCAAGAAACTGAAGAGTGTGAAA
GAGCTGCTGGGGATCACCATCATGGAAAGAAGCAGCTTCGAGAAGAATCCCATCGACTTTCTG
GAAGCCAAGGGCTACAAAGAAGTGAAAAAGGACCTGATCATCAAGCTGCCTAAGTACTCCCTG
TTCGAGCTGGAAAACGGCCGGAAGAGAATGCTGGCCTCTGCCGGCGAACTGCAGAAGGGAAAC
GAACTGGCCCTGCCCTCCAAATATGTGAACTTCCTGTACCTGGCCAGCCACTATGAGAAGCTG
AAGGGCTCCCCCGAGGATAATGAGCAGAAACAGCTGTTTGTGGAACAGCACAAGCACTACCTG
GACGAGATCATCGAGCAGATCAGCGAGTTCTCCAAGAGAGTGATCCTGGCCGACGCTAATCTG
GACAAAGTGCTGTCCGCCTACAACAAGCACCGGGATAAGCCCATCAGAGAGCAGGCCGAGAAT
ATCATCCACCTGTTTACCCTGACCAATCTGGGAGCCCCTGCCGCCTTCAAGTACTTTGACACC
ACCATCGACCGGAAGAGGTACACCAGCACCAAAGAGGTGCTGGACGCCACCCTGATCCACCAG
AGCATCACCGGCCTGTACGAGACACGGATCGACCTGTCTCAGCTGGGAGGTGAC

An exemplary amino acid sequence for ABE_7-Cas9(D10A) is set forth in SEQ ID NO: 159:

MSEVEFSHEYWMRHALTLAKRAWDEREVPVGAVLVHNNRVIGEGWNRPIGRHDPTAHAEIMAL
RQGGLVMQNYRLIDATLYVTLEPCVMCAGAMIHSRIGRVVFGARDAKTGAAGSLMDVLHHPGM
NHRVEITEGILADECAALLSDFFRMRRQEIKAQKKAQSSTDSGGSSGGSSGSETPGTSESATP
ESSGGSSGGSSEVEFSHEYWMRHALTLAKRARDEREVPVGAVLVLNNRVIGEGWNRAIGLHDP
TAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVFGVRNAKTGAAGSL
MDVLHYPGMNHRVEITEGILADECAALLCYFFRMPRQVFNAQKKAQSSTDSGGSSGGSSGSET
PGTSESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKK
NLIGALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVE
EDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIE
GDLNPDNSDVDKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKK
NGLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLS
DAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYA
GYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAIL

RRQEDFYPFLKDNREKIEKILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGA
SAQSFIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIV
DLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEEN
EDILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQS
GKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGIL
QTVKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPV
ENTQLQNEKLYLYYLQNGRDMYVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNR
GKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQI
TKHVAQILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLN
AVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLA
NGEIRKRPLIETNGETGEIVWDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNS
DKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPI
DFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHY
EKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQ
AENIIHLFTLTNLGAPAAFKYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD

An exemplary nucleic acid sequence encoding ABE_7-Cas9 (D10A) is set forth in SEQ ID NO: 160:

ATGTCCGAAGTCGAGTTTTCCCATGAGTACTGGATGAGACACGCATTGACTCTCGCAAAGAGG
GCTTGGGATGAACGCGAGGTGCCCGTGGGGGCAGTACTCGTGCATAACAATCGCGTAATCGGC
GAAGGTTGGAATAGGCCGATCGGACGCCACGACCCCACTGCACATGCGGAAATCATGGCCCTT
CGACAGGGAGGGCTTGTGATGCAGAATTATCGACTTATCGATGCGACGCTGTACGTCACGCTT
GAACCTTGCGTAATGTGCGCGGGAGCTATGATTCACTCCCGCATTGGACGAGTTGTATTCGGT
GCCCGCGACGCCAAGACGGGTGCCGCAGGTTCACTGATGGACGTGCTGCATCACCCAGGCATG
AACCACCGGGTAGAAATCACAGAAGGCATATTGGCGGACGAATGTGCGGCGCTGTTGTCCGAC
TTTTTTCGCATGCGGAGGCAGGAGATCAAGGCCCAGAAAAAAGCACAATCCTCTACTGACTCT
GGTGGTTCTTCTGGTGGTTCTAGCGGCAGCGAGACTCCCGGGACCTCAGAGTCCGCCACACCC
GAAAGTTCTGGTGGTTCTTCTGGTGGTTCTTCCGAAGTCGAGTTTTCCCATGAGTACTGGATG
AGACACGCATTGACTCTCGCAAAGAGGGCTCGAGATGAACGCGAGGTGCCCGTGGGGGCAGTA
CTCGTGCTCAACAATCGCGTAATCGGCGAAGGTTGGAATAGGGCAATCGGACTCCACGACCCC
ACTGCACATGCGGAAATCATGGCCCTTCGACAGGGAGGGCTTGTGATGCAGAATTATCGACTT
ATCGATGCGACGCTGTACGTCACGTTTGAACCTTGCGTAATGTGCGCGGGAGCTATGATTCAC
TCCCGCATTGGACGAGTTGTATTCGGTGTTCGCAACGCCAAGACGGGTGCCGCAGGTTCACTG
ATGGACGTGCTGCATTACCCAGGCATGAACCACCGGGTAGAAATCACAGAAGGCATATTGGCG
GACGAATGTGCGGCGCTGTTGTGTTACTTTTTTCGCATGCCCAGGCAGGTCTTTAACGCCCAG
AAAAAAGCACAATCCTCTACTGACTCTGGTGGTTCTTCTGGTGGTTCTAGCGGCAGCGAGACT
CCCGGGACCTCAGAGTCCGCCACACCCGAAAGTTCTGGTGGTTCTTCTGGTGGTTCTGATAAA
AAGTATTCTATTGGTTTAGCCATCGGCACTAATTCCGTTGGATGGGCTGTCATAACCGATGAA
TACAAAGTACCTTCAAAGAAATTTAAGGTGTTGGGGAACACAGACCGTCATTCGATTAAAAAG
AATCTTATCGGTGCCCTCCTATTCGATAGTGGCGAAACGGCAGAGGCGACTCGCCTGAAACGA
ACCGCTCGGAGAAGGTATACACGTCGCAAGAACCGAATATGTTACTTACAAGAAATTTTTAGC
AATGAGATGGCCAAAGTTGACGATTCTTTCTTTCACCGTTTGGAAGAGTCCTTCCTTGTCGAA
GAGGACAAGAAACATGAACGGCACCCCATCTTTGGAAACATAGTAGATGAGGTGGCATATCAT
GAAAAGTACCCAACGATTTATCACCTCAGAAAAAAGCTAGTTGACTCAACTGATAAAGCGGAC
CTGAGGTTAATCTACTTGGCTCTTGCCCATATGATAAAGTTCCGTGGGCACTTTCTCATTGAG
GGTGATCTAAATCCGGACAACTCGGATGTCGACAAACTGTTCATCCAGTTAGTACAAACCTAT

AATCAGTTGTTTGAAGAGAACCCTATAAATGCAAGTGGCGTGGATGCGAAGGCTATTCTTAGC
GCCCGCCTCTCTAAATCCCGACGGCTAGAAAACCTGATCGCACAATTACCCGGAGAGAAGAAA
AATGGGTTGTTCGGTAACCTTATAGCGCTCTCACTAGGCCTGACACCAAATTTTAAGTCGAAC
TTCGACTTAGCTGAAGATGCCAAATTGCAGCTTAGTAAGGACACGTACGATGACGATCTCGAC
AATCTACTGGCACAAATTGGAGATCAGTATGCGGACTTATTTTTGGCTGCCAAAAACCTTAGC
GATGCAATCCTCCTATCTGACATACTGAGAGTTAATACTGAGATTACCAAGGCGCCGTTATCC
GCTTCAATGATCAAAAGGTACGATGAACATCACCAAGACTTGACACTTCTCAAGGCCCTAGTC
CGTCAGCAACTGCCTGAGAAATATAAGGAAATATTCTTTGATCAGTCGAAAAACGGGTACGCA
GGTTATATTGACGGCGGAGCGAGTCAAGAGGAATTCTACAAGTTTATCAAACCCATATTAGAG
AAGATGGATGGGACGGAAGAGTTGCTTGTAAAACTCAATCGCGAAGATCTACTGCGAAAGCAG
CGGACTTTCGACAACGGTAGCATTCCACATCAAATCCACTTAGGCGAATTGCATGCTATACTT
AGAAGGCAGGAGGATTTTTATCCGTTCCTCAAAGACAATCGTGAAAAGATTGAGAAAATCCTA
ACCTTTCGCATACCTTACTATGTGGGACCCCTGGCCCGAGGGAACTCTCGGTTCGCATGGATG
ACAAGAAAGTCCGAAGAAACGATTACTCCATGGAATTTTGAGGAAGTTGTCGATAAAGGTGCG
TCAGCTCAATCGTTCATCGAGAGGATGACCAACTTTGACAAGAATTTACCGAACGAAAAAGTA
TTGCCTAAGCACAGTTTACTTTACGAGTATTTCACAGTGTACAATGAACTCACGAAAGTTAAG
TATGTCACTGAGGGCATGCGTAAACCCGCCTTTCTAAGCGGAGAACAGAAGAAAGCAATAGTA
GATCTGTTATTCAAGACCAACCGCAAAGTGACAGTTAAGCAATTGAAAGAGGACTACTTTAAG
AAAATTGAATGCTTCGATTCTGTCGAGATCTCCGGGGTAGAAGATCGATTTAATGCGTCACTT
GGTACGTATCATGACCTCCTAAAGATAATTAAAGATAAGGACTTCCTGGATAACGAAGAGAAT
GAAGATATCTTAGAAGATATAGTGTTGACTCTTACCCTCTTTGAAGATCGGGAAATGATTGAG
GAAAGACTAAAAACATACGCTCACCTGTTCGACGATAAGGTTATGAAACAGTTAAAGAGGCGT
CGCTATACGGGCTGGGGACGATTGTCGCGGAAACTTATCAACGGGATAAGAGACAAGCAAAGT
GGTAAAACTATTCTCGATTTTCTAAAGAGCGACGGCTTCGCCAATAGGAACTTTATGCAGCTG
ATCCATGATGACTCTTTAACCTTCAAAGAGGATATACAAAAGGCACAGGTTTCCGGACAAGGG
GACTCATTGCACGAACATATTGCGAATCTTGCTGGTTCGCCAGCCATCAAAAAGGGCATACTC
CAGACAGTCAAAGTAGTGGATGAGCTAGTTAAGGTCATGGGACGTCACAAACCGGAAAACATT
GTAATCGAGATGGCACGCGAAAATCAAACGACTCAGAAGGGGCAAAAAAACAGTCGAGAGCGG
ATGAAGAGAATAGAAGAGGGTATTAAAGAACTGGGCAGCCAGATCTTAAAGGAGCATCCTGTG
GAAAATACCCAATTGCAGAACGAGAAACTTTACCTCTATTACCTACAAAATGGAAGGGACATG
TATGTTGATCAGGAACTGGACATAAACCGTTTATCTGATTACGACGTCGATCACATTGTACCC
CAATCCTTTTTGAAGGACGATTCAATCGACAATAAAGTGCTTACACGCTCGGATAAGAACCGA
GGGAAAAGTGACAATGTTCCAAGCGAGGAAGTCGTAAAGAAAATGAAGAACTATTGGCGGCAG
CTCCTAAATGCGAAACTGATAACGCAAAGAAAGTTCGATAACTTAACTAAAGCTGAGAGGGGT
GGCTTGTCTGAACTTGACAAGGCCGGATTTATTAAACGTCAGCTCGTGGAAACCCGCCAAATC
ACAAAGCATGTTGCACAGATACTAGATTCCCGAATGAATACGAAATACGACGAGAACGATAAG
CTGATTCGGGAAGTCAAAGTAATCACTTTAAAGTCAAAATTGGTGTCGGACTTCAGAAAGGAT
TTTCAATTCTATAAAGTTAGGGAGATAAATAACTACCACCATGCGCACGACGCTTATCTTAAT
GCCGTCGTAGGGACCGCACTCATTAAGAAATACCCGAAGCTAGAAAGTGAGTTTGTGTATGGT
GATTACAAAGTTTATGACGTCCGTAAGATGATCGCGAAAAGCGAACAGGAGATAGGCAAGGCT
ACAGCCAAATACTTCTTTTATTCTAACATTATGAATTTCTTTAAGACGGAAATCACTCTGGCA
AACGGAGAGATACGCAAACGACCTTTAATTGAAACCAATGGGGAGACAGGTGAAATCGTATGG
GATAAGGGCCGGGACTTCGCGACGGTGAGAAAAGTTTTGTCCATGCCCCAAGTCAACATAGTA
AAGAAAACTGAGGTGCAGACCGGAGGGTTTTCAAAGGAATCGATTCTTCCAAAAAGGAATAGT
GATAAGCTCATCGCTCGTAAAAAGGACTGGGACCCGAAAAAGTACGGTGGCTTCGATAGCCCT
ACAGTTGCCTATTCTGTCCTAGTAGTGGCAAAAGTTGAGAAGGGAAAATCCAAGAAACTGAAG
TCAGTCAAAGAATTATTGGGGATAACGATTATGGAGCGCTCGTCTTTTGAAAAGAACCCCATC

GACTTCCTTGAGGCGAAAGGTTACAAGGAAGTAAAAAAGGATCTCATAATTAAACTACCAAAG
TATAGTCTGTTTGAGTTAGAAAATGGCCGAAAACGGATGTTGGCTAGCGCCGGAGAGCTTCAA
AAGGGGAACGAACTCGCACTACCGTCTAAATACGTGAATTTCCTGTATTTAGCGTCCCATTAC
GAGAAGTTGAAAGGTTCACCTGAAGATAACGAACAGAAGCAACTTTTTGTTGAGCAGCACAAA
CATTATCTCGACGAAATCATAGAGCAAATTTCGGAATTCAGTAAGAGAGTCATCCTAGCTGAT
GCCAATCTGGACAAAGTATTAAGCGCATACAACAAGCACAGGGATAAACCCATACGTGAGCAG
GCGGAAAATATTATCCATTTGTTTACTCTTACCAACCTCGGCGCTCCAGCCGCATTCAAGTAT
TTTGACACAACGATAGATCGCAAACGATACACTTCTACCAAGGAGGTGCTAGACGCGACACTG
ATTCACCAATCCATCACGGGATTATATGAAACTCGGATAGATTTGTCACAGCTTGGGGGTGA

An exemplary amino acid sequence for ABE_8-Cas9 (D10A) is set forth in SEQ ID NO: 161:

MKRTADGSEFESPKKKRKVSEVEFSHEYWMRHALTLAKRARDEREVPVGAVLVLNNRVIGEGW
NRAIGLHDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVFGVRN
SKRGAAGSLMNVLNYPGMNHRVEITEGILADECAALLCDFYRMPRQVFNAQKKAQSSINSGGS
SGGSSGSETPGTSESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAVITDEYKVPSKKFKVLG
NTDRHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFH
RLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMI
KFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRLENL
IAQLPGEKKNGLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYAD
LFLAAKNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIF
FDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQI
HLGELHAILRRQEDFYPFLKDNREKIEKILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWN
FEEVVDKGASAQSFIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFL
SGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLLKIIKD
KDFLDNEENEDILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLSRKL
INGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQVSGQGDSLHEHIANLAG
SPAIKKGILQTVKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRIEEGIKELG
SQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRLSDYDVDHIVPQSFLKDDSIDNK
VLTRSDKNRGKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIK
RQLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQFYKVREINNY
HHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMN
FFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSK
ESILPKRNSDKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIME
RSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQKGNELALPSKYV
NFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNK
HRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETR
IDLSQLGGD

An exemplary nucleic acid sequence encoding ABE_8-Cas9 (D10A) is set forth in SEQ ID NO: 162:

ATGAAACGGACAGCCGACGGAAGCGAGTTCGAGTCACCAAAGAAGAAGCGGAAAGTCTCTGAG
GTGGAGTTTTCCCACGAGTACTGGATGAGACATGCCCTGACCCTGGCCAAGAGGGCACGGGAT
GAGAGGGAGGTGCCTGTGGGAGCCGTGCTGGTGCTGAACAATAGAGTGATCGGCGAGGGCTGG
AACAGAGCCATCGGCCTGCACGACCCAACAGCCCATGCCGAAATTATGGCCCTGAGACAGGGC

GGCCTGGTCATGCAGAACTACAGACTGATTGACGCCACCCTGTACGTGACATTCGAGCCTTGC
GTGATGTGCGCCGGCGCCATGATCCACTCTAGGATCGGCCGCGTGGTGTTTGGCGTGAGGAAC
TCAAAAAGAGGCGCCGCAGGCTCCCTGATGAACGTGCTGAACTACCCCGGCATGAATCACCGC
GTCGAAATTACCGAGGGAATCCTGGCAGATGAATGTGCCGCCCTGCTGTGCGATTTCTATCGG
ATGCCTAGACAGGTGTTCAATGCTCAGAAGAAGGCCCAGAGCTCCATCAACTCCGGAGGATCT
AGCGGAGGCTCCTCTGGCTCTGAGACACCTGGCACAAGCGAGAGCGCAACACCTGAAAGCAGC
GGGGGCAGCAGCGGGGGGTCAGACAAGAAGTACAGCATCGGCCTGGCCATCGGCACCAACTCT
GTGGGCTGGGCCGTGATCACCGACGAGTACAAGGTGCCCAGCAAGAAATTCAAGGTGCTGGGC
AACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGAGCCCTGCTGTTCGACAGCGGCGAA
ACAGCCGAGGCCACCCGGCTGAAGAGAACCGCCAGAAGAAGATACACCAGACGGAAGAACCGG
ATCTGCTATCTGCAAGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCAC
AGACTGGAAGAGTCCTTCCTGGTGGAAGAGGATAAGAAGCACGAGCGGCACCCCATCTTCGGC
AACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCCCACCATCTACCACCTGAGAAAGAAA
CTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTGATCTATCTGGCCCTGGCCCACATGATC
AAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAG
CTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAAAACCCCATCAACGCCAGC
GGCGTGGACGCCAAGGCCATCCTGTCTGCCAGACTGAGCAAGAGCAGACGGCTGGAAAATCTG
ATCGCCCAGCTGCCCGGCGAGAAGAAGAATGGCCTGTTCGGAAACCTGATTGCCCTGAGCCTG
GGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGATGCCAAACTGCAGCTGAGC
AAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGAC
CTGTTTCTGGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGAGCGACATCCTGAGAGTGAAC
ACCGAGATCACCAAGGCCCCCCTGAGCGCCTCTATGATCAAGAGATACGACGAGCACCACCAG
GACCTGACCCTGCTGAAAGCTCTCGTGCGGCAGCAGCTGCCTGAGAAGTACAAAGAGATTTTC
TTCGACCAGAGCAAGAACGGCTACGCCGGCTACATTGACGGCGGAGCCAGCCAGGAAGAGTTC
TACAAGTTCATCAAGCCCATCCTGGAAAAGATGGACGGCACCGAGGAACTGCTCGTGAAGCTG
AACAGAGAGGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCCACCAGATC
CACCTGGGAGAGCTGCACGCCATTCTGCGGCGGCAGGAAGATTTTTACCCATTCCTGAAGGAC
AACCGGGAAAAGATCGAGAAGATCCTGACCTTCCGCATCCCCTACTACGTGGGCCCTCTGGCC
AGGGGAAACAGCAGATTCGCCTGGATGACCAGAAAGAGCGAGGAAACCATCACCCCCTGGAAC
TTCGAGGAAGTGGTGGACAAGGGCGCTTCCGCCCAGAGCTTCATCGAGCGGATGACCAACTTC
GATAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACC
GTGTATAACGAGCTGACCAAAGTGAAATACGTGACCGAGGGAATGAGAAAGCCCGCCTTCCTG
AGCGGCGAGCAGAAAAAGGCCATCGTGGACCTGCTGTTCAAGACCAACCGGAAAGTGACCGTG
AAGCAGCTGAAAGAGGACTACTTCAAGAAAATCGAGTGCTTCGACTCCGTGGAAATCTCCGGC
GTGGAAGATCGGTTCAACGCCTCCCTGGGCACATACCACGATCTGCTGAAAATTATCAAGGAC
AAGGACTTCCTGGACAATGAGGAAAACGAGGACATTCTGGAAGATATCGTGCTGACCCTGACA
CTGTTTGAGGACAGAGAGATGATCGAGGAACGGCTGAAAACCTATGCCCACCTGTTCGACGAC
AAAGTGATGAAGCAGCTGAAGCGGCGGAGATACACCGGCTGGGGCAGGCTGAGCCGGAAGCTG
ATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACAATCCTGGATTTCCTGAAGTCCGACGGC
TTCGCCAACAGAAACTTCATGCAGCTGATCCACGACGACAGCCTGACCTTTAAAGAGGACATC
CAGAAAGCCCAGGTGTCCGGCCAGGGCGATAGCCTGCACGAGCACATTGCCAATCTGGCCGGC
AGCCCCGCCATTAAGAAGGGCATCCTGCAGACAGTGAAGGTGGTGGACGAGCTCGTGAAAGTG
ATGGGCCGGCACAAGCCCGAGAACATCGTGATCGAAATGGCCAGAGAGAACCAGACCACCCAG
AAGGGACAGAAGAACAGCCGCGAGAGAATGAAGCGGATCGAAGAGGGCATCAAAGAGCTGGGC
AGCCAGATCCTGAAAGAACACCCCGTGGAAAACACCCAGCTGCAGAACGAGAAGCTGTACCTG
TACTACCTGCAGAATGGGCGGGATATGTACGTGGACCAGGAACTGGACATCAACCGGCTGTCC
GACTACGATGTGGACCATATCGTGCCTCAGAGCTTTCTGAAGGACGACTCCATCGACAACAAG

GTGCTGACCAGAAGCGACAAGAACCGGGGCAAGAGCGACAACGTGCCCTCCGAAGAGGTCGTG
AAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACGCCAAGCTGATTACCCAGAGAAAGTTC
GACAATCTGACCAAGGCCGAGAGAGGCGGCCTGAGCGAACTGGATAAGGCCGGCTTCATCAAG
AGACAGCTGGTGGAAACCCGGCAGATCACAAAGCACGTGGCACAGATCCTGGACTCCCGGATG
AACACTAAGTACGACGAGAATGACAAGCTGATCCGGGAAGTGAAAGTGATCACCCTGAAGTCC
AAGCTGGTGTCCGATTTCCGGAAGGATTTCCAGTTTTACAAAGTGCGCGAGATCAACAACTAC
CACCACGCCCACGACGCCTACCTGAACGCCGTCGTGGGAACCGCCCTGATCAAAAAGTACCCT
AAGCTGGAAAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGATCGCC
AAGAGCGAGCAGGAAATCGGCAAGGCTACCGCCAAGTACTTCTTCTACAGCAACATCATGAAC
TTTTTCAAGACCGAGATTACCCTGGCCAACGGCGAGATCCGGAAGCGGCCTCTGATCGAGACA
AACGGCGAAACCGGGGAGATCGTGTGGGATAAGGGCCGGGATTTTGCCACCGTGCGGAAAGTG
CTGAGCATGCCCCAAGTGAATATCGTGAAAAAGACCGAGGTGCAGACAGGCGGCTTCAGCAAA
GAGTCTATCCTGCCCAAGAGGAACAGCGATAAGCTGATCGCCAGAAAGAAGGACTGGGACCCT
AAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTATTCTGTGCTGGTGGTGGCCAAAGTG
GAAAAGGGCAAGTCCAAGAAACTGAAGAGTGTGAAAGAGCTGCTGGGGATCACCATCATGGAA
AGAAGCAGCTTCGAGAAGAATCCCATCGACTTTCTGGAAGCCAAGGGCTACAAAGAAGTGAAA
AAGGACCTGATCATCAAGCTGCCTAAGTACTCCCTGTTCGAGCTGGAAAACGGCCGGAAGAGA
ATGCTGGCCTCTGCCGGCGAACTGCAGAAGGGAAACGAACTGGCCCTGCCCTCCAAATATGTG
AACTTCCTGTACCTGGCCAGCCACTATGAGAAGCTGAAGGGCTCCCCCGAGGATAATGAGCAG
AAACAGCTGTTTGTGGAACAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAG
TTCTCCAAGAGAGTGATCCTGGCCGACGCTAATCTGGACAAAGTGCTGTCCGCCTACAACAAG
CACCGGGATAAGCCCATCAGAGAGCAGGCCGAGAATATCATCCACCTGTTTACCCTGACCAAT
CTGGGAGCCCCTGCCGCCTTCAAGTACTTTGACACCACCATCGACCGGAAGAGGTACACCAGC
ACCAAAGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGACACGG
ATCGACCTGTCTCAGCTGGGAGGTGAC

An exemplary amino acid sequence for ABE_VRQR- Cas9 (N) is set forth in SEQ ID NO: 163:

MKRTADGSEFESPKKKRKVSEVEFSHEYWMRHALTLAKRAWDEREVPVGAVLVHNNRVIGEGW
NRPIGRHDPTAHAEIMALRQGGLVMQNYRLIDATLYVTLEPCVMCAGAMIHSRIGRVVFGARD
AKTGAAGSLMDVLHHPGMNHRVEITEGILADECAALLSDFFRMRRQEIKAQKKAQSSTDSGGS
SGGSSGSETPGTSESATPESSGGSSGGSSEVEFSHEYWMRHALTLAKRARDEREVPVGAVLVL
NNRVIGEGWNRAIGLHDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRI
GRVVFGVRNAKTGAAGSLMDVLHYPGMNHRVEITEGILADECAALLCYFFRMPRQVFNAQKKA
QSSTDSGGSSGGSSGSETPGTSESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAVITDEYKV
PSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIFSNEM
AKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRL
IYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPINASGVDAKAILSARL
SKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLL
AQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQ
LPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTF
DNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILTFRIPYYVGPLARGNSRFAWMTRK
SEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVT
EGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTY
HDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYT
GWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQVSGQGDSL

HEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRERMKR
IEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRLSDYDVDHIVPQSF
LKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLS
ELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQF
YKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKATAK
YFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDFATVRKVLSMPQVNIVKKT
EVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGFVSPTVAYSVLVVAKVEKGKSKKLKSVK
ELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASARELQKGN
ELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVILADANL
DKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTIDRKQYRSTKEVLDATLIHQ
SITGLYETRIDLSQLGGDSGGSKRT

An exemplary nucleic acid sequence encoding ABE_VRQR –Cas9 (N) is set forth in SEQ ID NO: 164:

CTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAG
CTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGT
GAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATA
GGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGA
CAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGA
CCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATA
GCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACG
AACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGG
TAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATG
TAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTAT
TTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCG
GCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAA
AAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACACTCAGTGGAACGAAA
ACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAA
ATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACC
AATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCT
GACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAA
TGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAA
GGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCC
GGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAG
GCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAA
GGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCG
TTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTC
TTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCT
GAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGC
CACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAA
GGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAG
CATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAA
AGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAA
GCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAAC
AAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTCGACGGATCGGGAGATC
GATCTCCCGATCCCCTAGGGTCGACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCC

AGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAAATTTAAGCTA
CAACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGCGTTTTGCGC
TGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTATTAATAGT
AATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGG
TAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATG
TTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGTAAA
CTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTCAATG
ACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTGGC
AGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAATG
GGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGA
GTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGA
CGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTGGTTTAGTGAACC
GTCAGATCCGCTAGAGATCCGCGGCCGCTAATACGACTCACTATAGGGAGAGCCGCCACCATG
AAACGGACAGCCGACGGAAGCGAGTTCGAGTCACCAAAGAAGAAGCGGAAAGTCTCTGAAGTC
GAGTTTAGCCACGAGTATTGGATGAGGCACGCACTGACCCTGGCAAAGCGAGCATGGGATGAA
AGAGAAGTCCCCGTGGGCGCCGTGCTGGTGCACAACAATAGAGTGATCGGAGAGGGATGGAAC
AGGCCAATCGGCCGCCACGACCCTACCGCACACGCAGAGATCATGGCACTGAGGCAGGGAGGC
CTGGTCATGCAGAATTACCGCCTGATCGATGCCACCCTGTATGTGACACTGGAGCCATGCGTG
ATGTGCGCAGGAGCAATGATCCACAGCAGGATCGGAAGAGTGGTGTTCGGAGCACGGGACGCC
AAGACCGGCGCAGCAGGCTCCCTGATGGATGTGCTGCACCACCCCGGCATGAACCACCGGGTG
GAGATCACAGAGGGAATCCTGGCAGACGAGTGCGCCGCCCTGCTGAGCGATTTCTTTAGAATG
CGGAGACAGGAGATCAAGGCCCAGAAGAAGGCACAGAGCTCCACCGACTCTGGAGGATCTAGC
GGAGGATCCTCTGGAAGCGAGACACCAGGCACAAGCGAGTCCGCCACACCAGAGAGCTCCGGC
GGCTCCTCCGGAGGATCCTCTGAGGTGGAGTTTTCCCACGAGTACTGGATGAGACATGCCCTG
ACCCTGGCCAAGAGGGCACGCGATGAGAGGGAGGTGCCTGTGGGAGCCGTGCTGGTGCTGAAC
AATAGAGTGATCGGCGAGGGCTGGAACAGAGCCATCGGCCTGCACGACCCAACAGCCCATGCC
GAAATTATGGCCCTGAGACAGGGCGGCCTGGTCATGCAGAACTACAGACTGATTGACGCCACC
CTGTACGTGACATTCGAGCCTTGCGTGATGTGCGCCGGCGCCATGATCCACTCTAGGATCGGC
CGCGTGGTGTTTGGCGTGAGGAACGCAAAAACCGGCGCCGCAGGCTCCCTGATGGACGTGCTG
CACTACCCCGGCATGAATCACCGCGTCGAAATTACCGAGGGAATCCTGGCAGATGAATGTGCC
GCCCTGCTGTGCTATTTCTTTCGGATGCCTAGACAGGTGTTCAATGCTCAGAAGAAGGCCCAG
AGCTCCACCGACTCCGGAGGATCTAGCGGAGGCTCCTCTGGCTCTGAGACACCTGGCACAAGC
GAGAGCGCAACACCTGAAAGCAGCGGGGGCAGCAGCGGGGGGTCAGACAAGAAGTACAGCATC
GGCCTGGCCATCGGCACCAACTCTGTGGGCTGGGCCGTGATCACCGACGAGTACAAGGTGCCC
AGCAAGAAATTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGA
GCCCTGCTGTTCGACAGCGGCGAAACAGCCGAGGCCACCCGGCTGAAGAGAACCGCCAGAAGA
AGATACACCAGACGGAAGAACCGGATCTGCTATCTGCAAGAGATCTTCAGCAACGAGATGGCC
AAGGTGGACGACAGCTTCTTCCACAGACTGGAAGAGTCCTTCCTGGTGGAAGAGGATAAGAAG
CACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTACCCC
ACCATCTACCACCTGAGAAAGAAACTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTGATC
TATCTGGCCCTGGCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAAC
CCCGACAACAGCGACGTGGACAAGCTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTC
GAGGAAAACCCCATCAACGCCAGCGGCGTGGACGCCAAGGCCATCCTGTCTGCCAGACTGAGC
AAGAGCAGACGGCTGGAAAATCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAATGGCCTGTTC
GGAAACCTGATTGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCC
GAGGATGCCAAACTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCC
CAGATCGGCGACCAGTACGCCGACCTGTTTCTGGCCGCCAAGAACCTGTCCGACGCCATCCTG

CTGAGCGACATCCTGAGAGTGAACACCGAGATCACCAAGGCCCCCCTGAGCGCCTCTATGATC
AAGAGATACGACGAGCACCACCAGGACCTGACCCTGCTGAAAGCTCTCGTGCGGCAGCAGCTG
CCTGAGAAGTACAAAGAGATTTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATTGAC
GGCGGAGCCAGCCAGGAAGAGTTCTACAAGTTCATCAAGCCCATCCTGGAAAAGATGGACGGC
ACCGAGGAACTGCTCGTGAAGCTGAACAGAGAGGACCTGCTGCGGAAGCAGCGGACCTTCGAC
AACGGCAGCATCCCCCACCAGATCCACCTGGGAGAGCTGCACGCCATTCTGCGGCGGCAGGAA
GATTTTTACCCATTCCTGAAGGACAACCGGGAAAAGATCGAGAAGATCCTGACCTTCCGCATC
CCCTACTACGTGGGCCCTCTGGCCAGGGGAAACAGCAGATTCGCCTGGATGACCAGAAAGAGC
GAGGAAACCATCACCCCCTGGAACTTCGAGGAAGTGGTGGACAAGGGCGCTTCCGCCCAGAGC
TTCATCGAGCGGATGACCAACTTCGATAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCAC
AGCCTGCTGTACGAGTACTTCACCGTGTATAACGAGCTGACCAAAGTGAAATACGTGACCGAG
GGAATGAGAAAGCCCGCCTTCCTGAGCGGCGAGCAGAAAAAGGCCATCGTGGACCTGCTGTTC
AAGACCAACCGGAAAGTGACCGTGAAGCAGCTGAAAGAGGACTACTTCAAGAAAATCGAGTGC
TTCGACTCCGTGGAAATCTCCGGCGTGGAAGATCGGTTCAACGCCTCCCTGGGCACATACCAC
GATCTGCTGAAAATTATCAAGGACAAGGACTTCCTGGACAATGAGGAAAACGAGGACATTCTG
GAAGATATCGTGCTGACCCTGACACTGTTTGAGGACAGAGAGATGATCGAGGAACGGCTGAAA
ACCTATGCCCACCTGTTCGACGACAAAGTGATGAAGCAGCTGAAGCGGCGGAGATACACCGGC
TGGGGCAGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACAATC
CTGGATTTCCTGAAGTCCGACGGCTTCGCCAACAGAAACTTCATGCAGCTGATCCACGACGAC
AGCCTGACCTTTAAAGAGGACATCCAGAAAGCCCAGGTGTCCGGCCAGGGCGATAGCCTGCAC
GAGCACATTGCCAATCTGGCCGGCAGCCCCGCCATTAAGAAGGGCATCCTGCAGACAGTGAAG
GTGGTGGACGAGCTCGTGAAAGTGATGGGCCGGCACAAGCCCGAGAACATCGTGATCGAAATG
GCCAGAGAGAACCAGACCACCCAGAAGGGACAGAAGAACAGCCGCGAGAGAATGAAGCGGATC
GAAGAGGGCATCAAAGAGCTGGGCAGCCAGATCCTGAAAGAACACCCCGTGGAAAACACCCAG
CTGCAGAACGAGAAGCTGTACCTGTACTACCTGCAGAATGGGCGGGATATGTACGTGGACCAG
GAACTGGACATCAACCGGCTGTCCGACTACGATGTGGACCATATCGTGCCTCAGAGCTTTCTG
AAGGACGACTCCATCGACAACAAGGTGCTGACCAGAAGCGACAAGAACCGGGGCAAGAGCGAC
AACGTGCCCTCCGAAGAGGTCGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACGCC
AAGCTGATTACCCAGAGAAAGTTCGACAATCTGACCAAGGCCGAGAGAGGCGGCCTGAGCGAA
CTGGATAAGGCCGGCTTCATCAAGAGACAGCTGGTGGAAACCCGGCAGATCACAAAGCACGTG
GCACAGATCCTGGACTCCCGGATGAACACTAAGTACGACGAGAATGACAAGCTGATCCGGGAA
GTGAAAGTGATCACCCTGAAGTCCAAGCTGGTGTCCGATTTCCGGAAGGATTTCCAGTTTTAC
AAAGTGCGCGAGATCAACAACTACCACCACGCCCACGACGCCTACCTGAACGCCGTCGTGGGA
ACCGCCCTGATCAAAAAGTACCCTAAGCTGGAAAGCGAGTTCGTGTACGGCGACTACAAGGTG
TACGACGTGCGGAAGATGATCGCCAAGAGCGAGCAGGAAATCGGCAAGGCTACCGCCAAGTAC
TTCTTCTACAGCAACATCATGAACTTTTTCAAGACCGAGATTACCCTGGCCAACGGCGAGATC
CGGAAGCGGCCTCTGATCGAGACAAACGGCGAAACCGGGGAGATCGTGTGGGATAAGGGCCGG
GATTTTGCCACCGTGCGGAAAGTGCTGAGCATGCCCCAAGTGAATATCGTGAAAAAGACCGAG
GTGCAGACAGGCGGCTTCAGCAAAGAGTCTATCCTGCCCAAGAGGAACAGCGATAAGCTGATC
GCCAGAAAGAAGGACTGGGACCCTAAGAAGTACGGCGGCTTCGTGAGCCCCACCGTGGCCTAT
TCTGTGCTGGTGGTGGCCAAAGTGGAAAAGGGCAAGTCCAAGAAACTGAAGAGTGTGAAAGAG
CTGCTGGGGATCACCATCATGGAAAGAAGCAGCTTCGAGAAGAATCCCATCGACTTTCTGGAA
GCCAAGGGCTACAAAGAAGTGAAAAAGGACCTGATCATCAAGCTGCCTAAGTACTCCCTGTTC
GAGCTGGAAAACGGCCGGAAGAGAATGCTGGCCTCAGCCAGAGAACTGCAGAAGGGAAACGAA
CTGGCCCTGCCCTCCAAATATGTGAACTTCCTGTACCTGGCCAGCCACTATGAGAAGCTGAAG
GGCTCCCCCGAGGATAATGAGCAGAAACAGCTGTTTGTGGAACAGCACAAGCACTACCTGGAC
GAGATCATCGAGCAGATCAGCGAGTTCTCCAAGAGAGTGATCCTGGCCGACGCTAATCTGGAC

AAAGTGCTGTCCGCCTACAACAAGCACCGGGATAAGCCCATCAGAGAGCAGGCCGAGAATATC
ATCCACCTGTTTACCCTGACCAATCTGGGAGCCCCTGCCGCCTTCAAGTACTTTGACACCACC
ATCGACCGGAAGCAGTACAGAAGCACCAAAGAGGTGCTGGACGCCACCCTGATCCACCAGAGC
ATCACCGGCCTGTACGAGACACGGATCGACCTGTCTCAGCTGGGAGGTGACTCTGGCGGCTCA
AAAAGAACCG

A nucleic acid programmable DNA binding protein (napDNAbp), as used herein, refers to a protein that associates with a nucleic acid (*e.g.*, DNA or RNA), such as a guide nuclic acid, that guides the napDNAbp to a specific nucleic acid sequence. For example, a Cas9 protein can associate with a guide RNA that guides the Cas9 protein to a specific DNA sequence that has complementary to the guide RNA. In some embodiments, the napDNAbp is a Cas9 domain, for example a nuclease active Cas9, a Cas9 nickase (nCas9), or a nuclease inactive Cas9 (dCas9). Examples of nucleic acid programmable DNA binding proteins include, without limitation, Cas9 (*e.g.*, dCas9 and nCas9), CasX, CasY, Cpf1, C2c1, C2c2, C2C3, and Argonaute. Other nucleic acid programmable DNA binding proteins are also within the scope of this disclosure, though they may not be specifically listed in this disclosure.

A Cas9 or Cas9 domain refers to an RNA-guided nuclease comprising a Cas9 protein, or a fragment thereof (*e.g.*, a protein comprising an active, inactive, or partially active DNA cleavage domain of Cas9, and/or the gRNA binding domain of Cas9). A Cas9 nuclease is also referred to sometimes as a casn1 nuclease or a CRISPR (clustered regularly interspaced short palindromic repeat)-associated nuclease. CRISPR is an adaptive immune system that provides protection against mobile genetic elements (viruses, transposable elements and conjugative plasmids). CRISPR clusters contain spacers, sequences complementary to antecedent mobile elements, and target invading nucleic acids. CRISPR clusters are transcribed and processed into CRISPR RNA (crRNA). In type II CRISPR systems correct processing of pre-crRNA requires a trans-encoded small RNA (tracrRNA), endogenous ribonuclease 3 (rnc) and a Cas9 protein. The tracrRNA serves as a guide for ribonuclease 3-aided processing of pre-crRNA. Subsequently, Cas9/crRNA/tracrRNA endonucleolytically cleaves linear or circular dsDNA target complementary to the spacer. The target strand not complementary to crRNA is first cut endonucleolytically, then trimmed 3′-5′ exonucleolytically. In nature, DNA-binding and cleavage typically requires protein and both RNAs. However, single guide RNAs ("sgRNA", or simply "gNRA") can be engineered so as to incorporate aspects of both the crRNA and tracrRNA into a single RNA species. See, *e.g.*, Jinek M., Chylinski K., Fonfara I., Hauer M.,

Doudna J.A., Charpentier E. Science 337:816-821(2012), the entire contents of which is hereby incorporated by reference. Cas9 recognizes a short motif in the CRISPR repeat sequences (the PAM or protospacer adjacent motif) to help distinguish self versus non-self. Cas9 nuclease sequences and structures are well known to those of skill in the art (see, *e.g.*, "Complete genome sequence of an M1 strain of Streptococcus pyogenes." Ferretti et al., J.J., McShan W.M., Ajdic D.J., Savic D.J., Savic G., Lyon K., Primeaux C., Sezate S., Suvorov A.N., Kenton S., Lai H.S., Lin S.P., Qian Y., Jia H.G., Najar F.Z., Ren Q., Zhu H., Song L., White J., Yuan X., Clifton S.W., Roe B.A., McLaughlin R.E., Proc. Natl. Acad. Sci. U.S.A. 98:4658-4663(2001); "CRISPR RNA maturation by trans-encoded small RNA and host factor RNase III." Deltcheva E., Chylinski K., Sharma C.M., Gonzales K., Chao Y., Pirzada Z.A., Eckert M.R., Vogel J., Charpentier E., Nature 471:602-607(2011); and "A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity." Jinek M., Chylinski K., Fonfara I., Hauer M., Doudna J.A., Charpentier E. Science 337:816-821(2012), the entire contents of each of which are incorporated herein by reference). Cas9 orthologs have been described in various species, including, but not limited to, S. pyogenes and S. thermophilus. Additional suitable Cas9 nucleases and sequences will be apparent to those of skill in the art based on this disclosure, and such Cas9 nucleases and sequences include Cas9 sequences from the organisms and loci disclosed in Chylinski, Rhun, and Charpentier, "The tracrRNA and Cas9 families of type II CRISPR-Cas immunity systems" (2013) RNA Biology 10:5, 726-737; the entire contents of which are incorporated herein by reference. In some embodiments, a Cas9 nuclease has an inactive (*e.g.*, an inactivated) DNA cleavage domain, that is, the Cas9 is a nickase. Additional suitable nuclease-inactive dCas9 domains will be apparent to those of skill in the art based on this disclosure and knowledge in the field, and are within the scope of this disclosure.

An exemplary catalytically inactive Cas9 (dCas9):

DKKYSIGLAIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRL
KRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA
YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ
TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFK
SNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAP
LSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPI
LEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEK
ILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNE
KVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDY

FKKIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREM
IEERLKTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFM
QLIHDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPE
NIVIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGR
DMYVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW
RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN
DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV
YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEI
VWDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGFD
SPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL
PKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQ
HKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAF
KYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD (SEQ ID NO: 49)

An exemplary Cas9 nickase (nCas9):

DKKYSIGLAIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRL
KRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA
YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ
TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFK
SNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAP
LSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPI
LEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEK
ILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNE
KVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDY
FKKIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREM
IEERLKTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFM
QLIHDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPE
NIVIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGR
DMYVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW
RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN
DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV
YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEI
VWDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGFD
SPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL
PKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQ
HKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAF
KYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD (SEQ ID NO: 50)

A nuclease-inactivated Cas9 protein may interchangeably be referred to as a "dCas9" protein (for nuclease-"dead" Cas9). Methods for generating a Cas9 protein (or a fragment thereof) having an inactive DNA cleavage domain are known (See, *e.g.*, Jinek et al., Science. 337:816-821(2012); Qi et al., "Repurposing CRISPR as an RNA-Guided Platform for Sequence-Specific Control of Gene Expression" (2013) Cell. 28;152(5):1173-83, the entire

contents of each of which are incorporated herein by reference). For example, the DNA cleavage domain of Cas9 is known to include two subdomains, the HNH nuclease subdomain and the RuvC1 subdomain. The HNH subdomain cleaves the strand complementary to the gRNA, whereas the RuvC1 subdomain cleaves the non-complementary strand. Mutations within these subdomains can silence the nuclease activity of Cas9. For example, the mutations D10A and H840A completely inactivate the nuclease activity of S. pyogenes Cas9 (Jinek et al., Science. 337:816-821(2012); Qi et al., Cell. 28;152(5):1173-83 (2013)). In some embodiments, proteins comprising Cas9 or fragments thereof are referred to as "Cas9 variants." A Cas9 variant shares homology to Cas9, or a fragment thereof.

In some embodiments, the present disclosure provides Cas9 domains that have different PAM specificities. Typically, Cas9 proteins, such as Cas9 from S. pyogenes (spCas9), require a canonical NGG PAM sequence to bind a particular nucleic acid region, where the "N" in "NGG" is adenine (A), thymine (T), guanine (G), or cytosine (C), and the G is guanine. This may limit the ability to edit desired bases within a genome. In some embodiments, the base editing fusion proteins provided herein need to be positioned at a precise location, for example, where a target base is within a 4 base region (*e.g.*, a "deamination window"), which is approximately 15 bases upstream of the PAM. See Komor, A.C., et al., "Programmable editing of a target base in genomic DNA without double-stranded DNA cleavage" Nature 533, 420-424 (2016), the entire contents of which are hereby incorporated by reference. In some embodiments, the deamination window is within a 2, 3, 4, 5, 6, 7, 8, 9, or 10 base region. In some embodiments, the deamination window is 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 bases upstream of the PAM. Accordingly, in some embodiments, any of the fusion proteins provided herein may contain a Cas9 domain that is capable of binding a nucleotide sequence that does not contain a canonical (*e.g.*, NGG) PAM sequence. Cas9 domains that bind to non-canonical PAM sequences have been described in the art and would be apparent to the skilled artisan. For example, Cas9 domains that bind non-canonical PAM sequences have been described in Kleinstiver, B. P., et al., "Engineered CRISPR-Cas9 nucleases with altered PAM specificities" Nature 523, 481-485 (2015); and Kleinstiver, B. P., et al., "Broadening the targeting range of Staphylococcus aureus CRISPR-Cas9 by modifying PAM recognition" Nature Biotechnology 33, 1293-1298 (2015); the entire contents of each are

hereby incorporated by reference. In some embodiments, the non-canonical PAM is NGN or NAG. In some examples, the non-canonical PAM is AGA or CAG.

A deaminase or deaminase domain refers to a protein or enzyme that catalyzes a deamination reaction. In some embodiments, the deaminase is an adenosine deaminase, which catalyzes the hydrolytic deamination of adenine or adenosine. In some embodiments, the deaminase or deaminase domain is an adenosine deaminase, catalyzing the hydrolytic deamination of adenosine or deoxyadenosine to inosine or deoxyinosine, respectively. In some embodiments, the adenosine deaminase catalyzes the hydrolytic deamination of adenine or adenosine in deoxyribonucleic acid (DNA). The adenosine deaminases (*e.g.* engineered adenosine deaminases, evolved adenosine deaminases) provided herein may be from any organism, such as a bacterium. In some embodiments, the deaminase or deaminase domain is a variant of a naturally-occurring deaminase from an organism. In some embodiments, the deaminase or deaminase domain does not occur in nature. In some embodiments, the adenosine deaminase is from a bacterium, such as, E.coli, S. aureus, Bacillus subtilis, G. sulfurreducens, S. typhi, S. putrefaciens, H. influenzae, or C. crescentus. In some embodiments, the adenosine deaminase is a TadA deaminase. In some embodiments, the TadA deaminase is an E. coli TadA deaminase (ecTadA).

In some embodiments, the TadA deaminase is a full-length E. coli TadA deaminase. For example, in certain embodiments, the adenosine deaminase comprises the amino acid sequence:

MRRAFITGVFFLSEVEFSHEYWMRHALTLAKRAWDEREVPVGAVLVHNNRVIGEGWNRPIGRH DPTAHAEIMALRQGGLVMQNYRLIDATLYVTLEPCVMCAGAMIHSRIGRVVFGARDAKTGAAG SLMDVLHHPGMNHRVEITEGILADECAALLSDFFRMRRQEIKAQKKAQSSTD (SEQ ID NO: 52)

A linker, as used herein, refers to a bond (*e.g.*, covalent bond), chemical group, or a molecule linking two molecules or moieties, *e.g.*, two domains of a fusion protein, such as, for example, a nuclease-inactive Cas9 domain and a nucleic acid-editing domain (*e.g.*, an adenosine deaminase). In some embodiments, a linker joins a gRNA binding domain of an RNA-programmable nuclease, including a Cas9 nuclease domain, and the catalytic domain of a nucleic-acid editing protein. In some embodiments, a linker joins a dCas9 and a nucleic-acid editing protein. Typically, the linker is positioned between, or flanked by, two groups, molecules, or other moieties and connected to each one via a covalent bond, thus connecting

the two. In some embodiments, the linker is an amino acid or a plurality of amino acids (*e.g.*, a peptide or protein). In some embodiments, the linker is an organic molecule, group, polymer, or chemical moiety. In some embodiments, the linker is 5-100 amino acids in length, for example, 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, 30, 30-35, 35-40, 40-45, 45-50, 50-60, 60-70, 70-80, 80-90, 90-100, 100-150, or 150-200 amino acids in length. Longer or shorter linkers are also contemplated.

Some aspects of this disclosure provide complexes comprising any of the fusion proteins provided herein, and a guide nucleic acid bound to napDNAbp of the fusion protein. Some aspects of this disclosure provide complexes comprising any of the fusion proteins provided herein, and a guide RNA bound to a Cas9 domain (*e.g.*, a dCas9, a nuclease active Cas9, or a Cas9 nickase) of fusion protein.

In some embodiments, the guide nucleic acid (*e.g.*, guide RNA) is from 15-100 nucleotides long and comprises a sequence of at least 10 contiguous nucleotides that is complementary to a target sequence. In some embodiments, the guide RNA is 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 nucleotides long. In some embodiments, the guide RNA comprises a sequence of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40 contiguous nucleotides that is complementary to a target sequence. In some embodiments, the target sequence is a DNA sequence. In some embodiments, the target sequence is an RNA sequence. In some embodiments, the target sequence is a sequence in the genome of a mammal. In some embodiments, the target sequence is a sequence in the genome of a human. In some embodiments, the 3′ end of the target sequence is immediately adjacent to a canonical PAM sequence (NGG). In some embodiments, the guide nucleic acid (*e.g.*, guide RNA) is complementary to a sequence associated with a disease or disorder (*e.g.*, Usher Syndrome type 1F). In some embodiments, the guide nucleic acid (*e.g.*, guide RNA) is complementary to a sequence associated with a disease or disorder having a mutation in a gene (*e.g.*, PCDH15). In some embodiments, the mutation in PCDH15 is a point mutation. In other examples, the point mutation is selected from the point mutations in Table 1. Non-limiting exemplary guide RNA sequence are set forth in Table 4:

Guide	Editor	Sequence	PAM	SEQ ID NO
Guide 1	ABE7, max, 8e	TTC**A**CCTCTCATTCAGATTT	TGG	51

Guide 1 (-2)	ABE7, max, 8e	C**A**CCTCTCATTCAGATTT	TGG	165
Guide 1 (-1)	ABE7, max, 8e	TC**A**CCTCTCATTCAGATTT	TGG	166
Guide ALT	ABE7, max, 8e	GTGGTGGTTC**A**CCTCTCATT	CAG	167
Guide 1 (+1)	ABE7, max, 8e	GTTC**A**CCTCTCATTCAGATTT	TGG	168
Guide 1 (+2)	ABE7, max, 8e	GGTTC**A**CCTCTCATTCAGATT	TGG	169
Guide 1 (+3)	ABE7, max, 8e	TGGTTC**A**CCTCTCATTCAGATTT	TGG	170
Guide 2	ABE7, max, 8e	TC**A**CCTCTCATTCAGATTTT	GGG	171
Guide 3	ABEvrqr	TGGTGGTTC**A**CCTCTCATTC	AGA	172

In other embodiments, the guide RNA comprises a nucleic acid sequence at least 60%, 70%, 75%, 80%, 85%, 90%, 01%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to nucleic acid sequence of SEQ ID NO: 51, and 165-172. The gRNA sequences provided herein are sequences that encode RNA that can direct Cas9, or any of the base editors provided herein, to a target site. For example, the gRNA sequences provided herein may be cloned into a gRNA expression vector, such as pFYF to encode a gRNA that targets Cas9, or any of the base editors provided herein, to a target site in order to correct a disease-related mutation. It should be appreciated, however, that additional mutations may be corrected to treat additional diseases associated with a G to A or C to T mutation. Furthermore, additional gRNAs may be designed based on the disclosure and the knowledge in the art, which would be appreciated by the skilled artisan.

In some embodiments, the purpose of the methods provided herein is to restore the function of a dysfunctional gene (*e.g., PCDH15*) via genome editing. The nucleobase editing proteins provided herein can be validated for gene editing-based human therapeutics in vitro, *e.g.*, by correcting a disease-associated mutation in human cell culture. It will be understood by the skilled artisan that the nucleobase editing proteins provided herein, *e.g.,* the base editor comprising a nucleic acid programmable DNA binding protein (*e.g.*, Cas9) and an adenosine deaminase domain can be used to correct any single point G to A or C to T mutation. In some embodiments deamination of the A that is base-paired with the mutant T, followed by a round of replication, corrects the mutation. Exemplary point mutations that can be corrected are listed in Tables 1.

The successful correction of point mutations in disease-associated genes and alleles opens up new strategies for gene correction with applications in therapeutics and basic research for diseases (*e.g.,* somatic recessive congenital diseases such as Usher Syndrome type 1F). Site-specific single-base modification systems like the disclosed fusions of a nucleic acid

programmable DNA binding protein and an adenosine deaminase domain can be used to restore protein function in vitro, ex vivo, or in vivo.

The instant disclosure provides methods for the treatment of a subject diagnosed with a disease (*e.g.,* Usher Syndrome type 1F) associated with or caused by a point mutation of a gene (*e.g.,* c. C733>T in *PCDH15*) that can be corrected by a DNA editing fusion protein provided herein. For example, in some embodiments, a method is provided that comprises administering to a subject having such a disease, *e.g.*, Usher Syndrome type 1F, an effective amount of an adenosine deaminase fusion protein that corrects the point mutation or introduces a deactivating mutation into a disease-associated gene.

V. Kits and Related Composition

The agents described herein may, in some embodiments, be assembled into pharmaceutical or diagnostic or research kits to facilitate their use in therapeutic, diagnostic or research applications. A kit may include one or more containers housing the components of the disclosure and instructions for use. Specifically, such kits may include one or more agents described herein, along with instructions describing the intended application and the proper use of these agents. In certain embodiments agents in a kit may be in a pharmaceutical formulation and dosage suitable for a particular application and for a method of administration of the agents. Kits for research purposes may contain the components in appropriate concentrations or quantities for running various experiments.

In some embodiments, the instant disclosure relates to a kit for producing a rAAV, the kit comprising a container housing an isolated nucleic acid comprising a transgene encoding a protein (*e.g.*, mini-PCDH15) having the amino acid sequence set forth in SEQ ID NO: 31, 33, 35, 37, 39, 41, 43, or 45. In some embodiments, the kit further comprises a container housing an isolated nucleic acid encoding an AAV capsid protein, for example, an AAV.PHP.B capsid protein (*e.g.*, SEQ ID NO: 47).

In some embodiments, the instant disclosure relates to a kit for treating hearing loss and/or blindness. In some embodiments, the kit is for delivering a functional protein (*e.g.*, mini-PCDH15) to a target cell (*e.g.*, inner hair cell, out hair cell or photoreceptor) using gene therapy (*e.g.*, rAAV described herein). In other embodiments, the kit is for correcting a

mutation in a disease related gene (*e.g.,* c.722C>T in *PCDH15* gene in Usher Syndrome type 1F) using a base editor described herein.

The kit may be designed to facilitate use of the methods described herein by researchers and can take many forms. Each of the compositions of the kit, where applicable, may be provided in liquid form (*e.g.*, in solution), or in solid form, (*e.g.*, a dry powder). In certain cases, some of the compositions may be constitutable or otherwise processable (*e.g.*, to an active form), for example, by the addition of a suitable solvent or other species (for example, water or a cell culture medium), which may or may not be provided with the kit. As used herein, "instructions" can define a component of instruction and/or promotion, and typically involve written instructions on or associated with packaging of the disclosure. Instructions also can include any oral or electronic instructions provided in any manner such that a user will clearly recognize that the instructions are to be associated with the kit, for example, audiovisual (*e.g.*, videotape, DVD, etc.), Internet, and/or web-based communications, etc. The written instructions may be in a form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which instructions can also reflects approval by the agency of manufacture, use or sale for animal administration.

The kit may contain any one or more of the components described herein in one or more containers. As an example, in one embodiment, the kit may include instructions for mixing one or more components of the kit and/or isolating and mixing a sample and applying to a subject. The kit may include a container housing agents described herein. The agents may be in the form of a liquid, gel or solid (powder). The agents may be prepared sterilely, packaged in syringe and shipped refrigerated. Alternatively it may be housed in a vial or other container for storage. A second container may have other agents prepared sterilely. Alternatively the kit may include the active agents premixed and shipped in a syringe, vial, tube, or other container.

Exemplary embodiments of the invention will be described in more detail by the following examples. These embodiments are exemplary of the invention, which one skilled in the art will recognize is not limited to the exemplary embodiments.

VI. General techniques

The practice of the present invention will employ, unless otherwise indicated,

conventional techniques of molecular biology (including recombinant techniques), microbiology, cell biology, biochemistry and immunology, which are within the skill of the art. Molecular Cloning: A Laboratory Manual, second edition (Sambrook, *et al.*, 1989) Cold Spring Harbor Press; Oligonucleotide Synthesis (M. J. Gait, ed., 1984); Methods in Molecular Biology, Humana Press; Cell Biology: A Laboratory Notebook (J. E. Cellis, ed., 1998) Academic Press; Animal Cell Culture (R. I. Freshney, ed., 1987); Introduction to Cell and Tissue Culture (J. P. Mather and P. E. Roberts, 1998) Plenum Press; Cell and Tissue Culture: Laboratory Procedures (A. Doyle, J. B. Griffiths, and D. G. Newell, eds., 1993-8) J. Wiley and Sons; Methods in Enzymology (Academic Press, Inc.); Handbook of Experimental Immunology (D. M. Weir and C. C. Blackwell, eds.); Gene Transfer Vectors for Mammalian Cells (J. M. Miller and M. P. Calos, eds., 1987); Current Protocols in Molecular Biology (F. M. Ausubel, *et al.*, eds., 1987); PCR: The Polymerase Chain Reaction, (Mullis, *et al.*, eds., 1994); Current Protocols in Immunology (J. E. Coligan *et al.*, eds., 1991); Short Protocols in Molecular Biology (Wiley and Sons, 1999); Immunobiology (C. A. Janeway and P. Travers, 1997); Antibodies (P. Finch, 1997); Antibodies: a practical approach (D. Catty., ed., IRL Press, 1988-1989); Monoclonal antibodies: a practical approach (P. Shepherd and C. Dean, eds., Oxford University Press, 2000); Using antibodies: a laboratory manual (E. Harlow and D. Lane (Cold Spring Harbor Laboratory Press, 1999); The Antibodies (M. Zanetti and J. D. Capra, eds., Harwood Academic Publishers, 1995).Without further elaboration, it is believed that one skilled in the art can, based on the above description, utilize the present invention to its fullest extent. The following specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever. All publications cited herein are incorporated by reference for the purposes or subject matter referenced herein.

Without further elaboration, it is believed that one skilled in the art can, based on the above description, utilize the present invention to its fullest extent. The following specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever. All publications cited herein are incorporated by reference for the purposes or subject matter referenced herein.

EXAMPLES

Example 1: mini-PCDH15 Proteins Encoded by a Single AAV Genome for Rescue of Hair Cell Function

In hair cells, the PCDH15 protein forms the 'tip link' between stereocilia (Kazmierczak et al., 2007), pulling directly on ion channels to initiate the electrical response to sound (FIG. 1A). PCDH15 is a large protein of up to 1955 amino acids, forming 11 link-like 'extracellular cadherin' (EC) repeats and a transmembrane domain (Ahmed et al., 2001; Ge et al., 2018). The X-ray crystal structure of the PCDH15 extracellular domain has been solved by our collaborator Marcos Sotomayor (Sotomayor et al., 2012; Araya-Secchi et al., 2016; Powers et al., 2017; Narui and Sotomayor, 2018; De-la-Torre et al., 2018).

miniPCDH15 constructs based on a number of considerations: structure of full-length hsPCDH15; non-canonical linkers at EC5-6, EC9-10 and EC8-9; retention of EC1-3 for interactions with CDH23 (EC1-2) and parallel dimerization (EC2-3); retention of EC11-MAD12 for parallel dimerization and interactions with transmembrane proteins. Accordingly eight versions of msPCDH15 with 3-5 EC domain deletions were generated. Each expression vector includes miniPCDH15-IRES-GFP such that GFP expression can be used for detection. (FIG. 1B). Each miniPCDH15 coding sequence encodes CD2 splice form of PCDH15, which is necessary for hair-cell function. The deletion of 3-5 EC domains from PCDH15 coding sequence decreased the size of the coding sequence from ~5400 bp to 3750-4400 bp, rendering it amenable to be packaged into a single AAV vector (FIG. 1C). Both mouse mini-PCDH15 and human mini-PCDH15 were designed such that V1 lacks EC4, EC7 and EC8 domains; V2 lacks EC5, EC6 and EC7 domains; V3 lacks EC4, EC5, EC6 and EC7 domains; V4 lacks EC4, EC5, EC6, EC7, and EC8; V5 lacks EC4, EC8, EC9, and EC10; V6 lacks EC5, EC6, EC9, and EC10; V7 lacks EC4, EC5, EC6, EC9, and EC10; and V8 lacks EC5, EC6, EC8, EC9, and EC10 (FIGs. 1D-1F). One skilled in the art would readily understood that these exemplary mini-PCDH15s are not meant to be limiting and other mini-PCDH15s can be designed by deletion of different EC domains.

Human mini-PCDH15 amino acid sequences and nucleic acid coding sequences are set forth as follows: V1 (SEQ ID NO: 31 and SEQ ID NO: 32; SEQ ID NO: 75 and SEQ ID NO: 77; SEQ ID NO: 76 and SEQ ID NO: 78); V2 (SEQ ID NO: 33 and SEQ ID NO: 34; SEQ ID NO: 79 and SEQ ID NO: 81; SEQ ID NO: 80 and SEQ ID NO: 82); V3 (SEQ ID NO: 35 and

SEQ ID NO: 36; SEQ ID NO: 83 and SEQ ID NO: 85; SEQ ID NO: 84 and SEQ ID NO: 86); V4 (SEQ ID NO: 41 and SEQ ID NO: 42; SEQ ID NO: 95 and SEQ ID NO: 97; SEQ ID NO: 96 and SEQ ID NO: 98); V5 (SEQ ID NO: 37 and SEQ ID NO: 38; SEQ ID NO: 87 and SEQ ID NO: 89; SEQ ID NO: 88 and SEQ ID NO: 90); V6 (SEQ ID NO: 39 and SEQ ID NO: 40; SEQ ID NO: 91 and SEQ ID NO: 93; SEQ ID NO: 92 and SEQ ID NO: 94); V7 (SEQ ID NO: 43 and SEQ ID NO: 44; SEQ ID NO: 99 and SEQ ID NO: 101; SEQ ID NO: 100 and SEQ ID NO: 102); V8 (SEQ ID NO: 45 and SEQ ID NO: 46; SEQ ID NO: 103 and SEQ ID NO: 105; SEQ ID NO: 104 and SEQ ID NO: 106), V9 (SEQ ID NO: 71 and SEQ ID NO: 72; SEQ ID NO: 107 and SEQ ID NO: 109; SEQ ID NO: 108 and SEQ ID NO: 110) and V10 (SEQ ID NO: 73 and SEQ ID NO: 74; SEQ ID NO: 111 and SEQ ID NO: 113; SEQ ID NO: 112 and SEQ ID NO: 114).

Mouse mini-PCDH15 coding sequences are as follows:

Mouse mini-PCDH15-CD2-1-V1

AAGGGCTGTGTTGTAACCTTCGGAGTTTGCGCCTGGAGATTTCTTGGGCTCTTCATCCTTCCT
TCTGTCATATTCTGGCACCTGAAAGCCCCAGGGGCCTCCGGAGAGACTCTCACTGGTACTGCT
GCTGCTGCTCAGTTCTGACTCTGACTCCTCACTTTCCACGCCCCTCTCCATGGAGACTGATTC
TGCACTGCCCTCCTCTGGGACATCCTGAGCCTCCAGGTCTGTGGACTCATCCATGGGAGCTGC
TTCGCTTTCTTCTCCTTCCTCTGCCCGTTCTTCCTCCTCTAGTGGGGGCTCTTCTTCCTCTTC
CACCGGGGGCTCCTCTCTCTTACCTTTCACCTCCTGGATTTCCTCGACCACAGGCCTTCTTCT
AGCCAGCACGATGTTTTTTCTTGCTTTCTCTCCCTCTGACTCAGTGGACTCAGACTCCTCTGA
CTCCGGGGTAGAGCTCTCCTCCGCTTCCTCAGATGGGGTCTCCGACTCTGATTCTTCAGTTGT
CTCGGACTCGCTGAACTCGGACTCCGTTTCTGTGTATTCTGTGTAGTCGCTGGACTCCTCCTC
TGACTCCACGGTGCTTTCGGTAGCTTCCTCCTGGTCTAGAGTCAGTTGAAGATAGTCTTTGTC
TTCTTCATCAAGGCGCCTCCTCCACTCCTCGCCCTCAAGGTCAATGCCTCTTTTCTCAGCGAG
ACCTCTGACTTTCTTAAAAATCATCGGGAATATCCTGGCTCTCTTCCACGTTGGGTATGTGGG
CTCAGCCGCTGGTGGCTTCTCAACGGTGACTACCACCTCCTCCTCACTAGGCTCTCTAATTTC
AACTTTGGGTTTTTTAACTTTCTCTGGCTCTACCTCTTCTTCTTCATATTCCTCTTCAGCTTC
ACCAATGACTTCGCCGTATTCCTCCTGTCCAGCAGGTGGCAGCAGTCGACGGCGACTTCCATA
CTGGGGCATCTCATACTTATGCATTGCGCTCTCTCCCAGTTCTTCATAGAGATGTGCTCCTGG
TGGTGGTGGTGGCGGGGGCGGGGGCGGCGCAGGCGCAGCTGGTACAGGAGCTGCAGGCTTGGC
TGCAGGCATAGCAGACTGAATTCTTGCGGTCTTCGTGCACTCAGCCTGGCGTACTTTAAACTG
TCGGTAGCTTACTAAGACGACCAAGATGGCTGGGATGCAACAGAGGATGATGATGAAGGCCAA
GGCCAGCAAGGCCCCTTCTGTGTACCCCAAGCTTTCTCCTCGCTTCTTGATGCTCGTCACTGC
CTCAGGTGTCCGAATCTCCAGAATGCGCCCTCCTTCCCCGTAATACGGCTGGAAGTCTTTATT
GATATCGAGCAGTTTGCCGTCCAGGAACTTAAAAAGCTCATTTCTGTCGATGGCTCTGTTGGT
CTGCGGGTCGATGGCATAGACAGTCAGGTCGCACTTGCTATAGTCTTCTAGGGAGTAGGCGTC
TCCATGGCGACGGGCACCTATGGACTCCACCACAACCTTGGCACCAGGAATTTGCTCCTGAAC
GTAGCGATCCAAAATCTCTGTAAGGTCTTCTATCTTCTTTTCCACTAGTGTAGGGGGCACATT
GGAGACAATGACCTGCATATCCAGTTGATTGACCACGGAGACCAGTACGTCTGCTTTCCCGCT
CAACCCCTTCCCGTAGTCGTCAGTTGCAATCACTTGAAACTTGAAGTAGGATCTTCTCATATT

GTGGAAGAGCATGGCTGTCTTGATGAGACCTGTGTATGTTTCCACCACAAACCCCTCTTTGCC
CTCTTTAATCGGCGGTATGATGAGCCGGTAGGCCATGGCACTGTAATTACCCGTGTCCCTGTC
GGTGGCCTTCACTCTGAGCACAGATGCGAACATCCTTGCGTCTTCAGACACACCTCCAATGTA
GAATTTCTTCTGGAACACTGGGGGGTGATCGTTTTCATCCTGAATCTCAATGTACACCTTAGC
TGTATTGCTTTTTGAAGGGACTCGGAGATTGGCAAGGACCACTTCCAGAGAATCTGCTTGTAC
CCGGAGCACATAGCTGGTCCTTGTCTCGTAATCCAATGGTGAATTCACATAGATGACCCCAGT
GACATTGTTGATTCCAAACTTGTCTTCCTCATTTCCTGCCACAATGGAGTACACGATGCTCTG
ATTAATGGCAGCAGCAGAAATGACACCAACTACAGTCCCTCTGGCCGCAAGCTCACTTACAGG
AGGAGGTCTGTATTCCTCTTGGGTGAAGCGTGGGATCTCTCCAGGATGTAAGACAAGAATTCT
CACCGTGGCACTGCTGGACATCACAGGTTCGCCGTCATCAAAAGCCACAACCACCAGCTTGAA
AATCGTAGTAGGCTCTTCATTAAGATTGACGCGGGTTACTACTCTTCCAGAATCTTCCTCTAC
ATCAAAAATACTGGCTGGGTATGGAAACTGCACGTCGTCCACTCGATACCTCACCCTACTTGC
AGGCATCCCAGGTGGGTCCGCATCTTCAGCATAAACGGTGGTGATTGGTGTCCCCTTGACTGC
ATCTGGAGCCACCATCCCCTTGTAGATGCGTTTGCTAAACACTGGAGGGTTGTCATTGACGTC
CGTCACCACTATGTTCACAGTGGCAGTTGAGGTTCCATCCGGTCTGCCATCTGAGGCTGTGAC
GATGAGGATGTAGCGGTCTGTGCTCTCGCGGTCTAGAGCCTTCCCTAGGCTGAGAATCCCTGT
GGTTTCTGAAAGATTAAAAACTCTCTGAGGGTCTCCATTCTCGATGGCATATGTGATTGGATC
TCCCTCTCGATCAGTTGCCTGTAGATTTAATAAAATAGCACCGATCCTCATGGCCTCGCTGAC
TTCCAGACTGTACATCAGCTGCGGGAAGCGGGGAGGGCTCTGGTTGTTAGGAGGAAGCACCTC
GATGTACACTGTGCAGATGGAGTGCCTTCTTTCTGCAGGCGGGGCGTTGTCCGAAGCCTGCAC
TGTGAGCGCATACGTCTGTCCCACGATCAGCTCCACGCCTGGTGCAATGCTCACCAGCCCTGT
GGTCTTGTTGATCACGAAGTCTCCCTTGCCCCCCACCAGTATTTCATAGGAGATCTCCCCATT
AGAGCCTTCATCAGCATCTACCGCTGTCAGCTGAATGACGCTGTCCCCAGGACTCATGTCTGT
GTAAACATAGACATCATAGGAGATTTCAGGGAAGGTGGGCGTCTGATTGTTTTCGTCTAGTAT
TTCGATGTGCAGACTAGCAAAGGCAGGAAGTGGGTGGCCATTGTCCTGCTCAGCCTTAATAAC
CAAATCAAATTTTTGATGGAAGTCTCTGTTTACTGGCTCCAGGAGAGTGAGTTCTGCAGTCCT
GGGATGCATATGGAAGAAGCGGGGGTAATCCTCAGGGGTGCCGACAAGGATGGAGTAGAGGAT
GCCAGGTCGATCAGATGGTGGTTGGATGTTTCGGTCCTGATCAATGGCTTGGATAGGTGGTGT
CACCAAAATAGGGTTCAGTTCTTCCGGAGTCCTCAGTTCAGGAATGGCAGCTTGGTAGGTGAG
TGGACGACAGTCACGTGTGTTTGGCACAAGAACACAAGGCAGAAACATAGGTCCCAGGTCATC
TCCATCTAGAACATCTACTGTGAGGGTGGTGGTGGTTGTTCGCCTCTCATTCAGATTTTGTGC
ACGGTCATTTGCTTGGATGATGACATAGTAGCGAGTCTTATCCTCATAGTTGAGTCTTTTCCT
CAGTACCACGTTGCCAGTCAGCATGAGTGGAATTTCAAAGGTGTCGTTGGATGTCGGATCTTC
TGGGTTGTACTGAATCACGTATTCTATCTGTCCATTAGGGCCATCGTCTATGTCTGTAGCTCC
ATTGTCTCCCGAGAACCCCGTGAATATCGTGGTGCCAACTGGAGTGAGCTCATTCACGGTGGC
ATAGTAGCTTTCATGCTTGAATGTGGGGGAGTTGTCATTCCGATCTCGCACCACGATGCGTAC
TTCATGATAGATAACTGTGCCAACCTTCTTGTTGACACACTGGACTTGCACCACAATGGAGTG
TATGTTCATTGGTGGGTCTCTATCCAGAACTCTTCCGGTACTGTTCAGGAAAAGCATCTGTTT
AACGGGGTCCAGCAACACCCAGTAGTCCACGTTGTCCTTTAAAGAGAGCTCTATGGTGGGGTC
TGGTCCTCCGGCAGTCCCCTTAATCAACATGTTATCCACCAGAATTGTACCGTTTCGACTCTC
TTCATCAATGGCCACGATAGTAGCTGGTGGTCCTCCCCTAGCTAGTTTGCAATCCTCGTATTG
CCAGTCATCGTCATACTGGCCCCAGCTGACTACCAAGAGAGAGGCAATGAGGATCCCATGGGG
TAAACACTTCCAGACAGCAAACTGTAGGAACAT (SEQ ID NO: 150)

Mouse mini-PCDH15-CD2-1-V2

AAGGGCTGTGTTGTAACCTTCGGAGTTTGCGCCTGGAGATTTCTTGGGCTCTTCATCCTTCCT
TCTGTCATATTCTGGCACCTGAAAGCCCCAGGGGCCTCCGGAGAGACTCTCACTGGTACTGCT
GCTGCTGCTCAGTTCTGACTCTGACTCCTCACTTTCCACGCCCCTCTCCATGGAGACTGATTC
TGCACTGCCCTCCTCTGGGACATCCTGAGCCTCCAGGTCTGTGGACTCATCCATGGGAGCTGC
TTCGCTTTCTTCTCCTTCCTCTGCCCGTTCTTCCTCCTCTAGTGGGGGCTCTTCTTCCTCTTC
CACCGGGGGCTCCTCTCTCTTACCTTTCACCTCCTGGATTTCCTCGACCACAGGCCTTCTTCT
AGCCAGCACGATGTTTTTTCTTGCTTTCTCTCCCTCTGACTCAGTGGACTCAGACTCCTCTGA
CTCCGGGGTAGAGCTCTCCTCCGCTTCCTCAGATGGGGTCTCCGACTCTGATTCTTCAGTTGT
CTCGGACTCGCTGAACTCGGACTCCGTTTCTGTGTATTCTGTGTAGTCGCTGGACTCCTCCTC
TGACTCCACGGTGCTTTCGGTAGCTTCCTCCTGGTCTAGAGTCAGTTGAAGATAGTCTTTGTC
TTCTTCATCAAGGCGCCTCCTCCACTCCTCGCCCTCAAGGTCAATGCCTCTTTTCTCAGCGAG
ACCTCTGACTTTCTTAAAAATCATCGGGAATATCCTGGCTCTCTTCCACGTTGGGTATGTGGG
CTCAGCCGCTGGTGGCTTCTCAACGGTGACTACCACCTCCTCCTCACTAGGCTCTCTAATTTC
AACTTTGGGTTTTTTAACTTTCTCTGGCTCTACCTCTTCTTCTTCATATTCCTCTTCAGCTTC
ACCAATGACTTCGCCGTATTCCTCCTGTCCAGCAGGTGGCAGCAGTCGACGGCGACTTCCATA
CTGGGGCATCTCATACTTATGCATTGCGCTCTCTCCCAGTTCTTCATAGAGATGTGCTCCTGG
TGGTGGTGGTGGCGGGGGCGGGGGCGGCGCAGGCGCAGCTGGTACAGGAGCTGCAGGCTTGGC
TGCAGGCATAGCAGACTGAATTCTTGCGGTCTTCGTGCACTCAGCCTGGCGTACTTTAAACTG
TCGGTAGCTTACTAAGACGACCAAGATGGCTGGGATGCAACAGAGGATGATGATGAAGGCCAA
GGCCAGCAAGGCCCCTTCTGTGTACCCCAAGCTTTCTCCTCGCTTCTTGATGCTCGTCACTGC
CTCAGGTGTCCGAATCTCCAGAATGCGCCCTCCTTCCCCGTAATACGGCTGGAAGTCTTTATT
GATATCGAGCAGTTTGCCGTCCAGGAACTTAAAAAGCTCATTTCTGTCGATGGCTCTGTTGGT
CTGCGGGTCGATGGCATAGACAGTCAGGTCGCACTTGCTATAGTCTTCTAGGGAGTAGGCGTC
TCCATGGCGACGGGCACCTATGGACTCCACCACAACCTTGGCACCAGGAATTTGCTCCTGAAC
GTAGCGATCCAAAATCTCTGTAAGGTCTTCTATCTTCTTTTCCACTAGTGTAGGGGGCACATT
GGAGACAATGACCTGCATATCCAGTTGATTGACCACGGAGACCAGTACGTCTGCTTTCCCGCT
CAACCCCTTCCCGTAGTCGTCAGTTGCAATCACTTGAAACTTGAAGTAGGATCTTCTCATATT
GTGGAAGAGCATGGCTGTCTTGATGAGACCTGTGTATGTTTCCACCACAAACCCCTCTTTGCC
CTCTTTAATCGGCGGTATGATGAGCCGGTAGGCCATGGCACTGTAATTACCCGTGTCCCTGTC
GGTGGCCTTCACTCTGAGCACAGATGCGAACATCCTTGCGTCTTCAGACACACCTCCAATGTA
GAATTTCTTCTGGAACACTGGGGGGTGATCGTTTTCATCCTGAATCTCAATGTACACCTTAGC
TGTATTGCTTTTTGAAGGGACTCGGAGATTGGCAAGGACCACTTCCAGAGAATCTGCTTGTAC
CCGGAGCACATAGCTGGTCCTTGTCTCGTAATCCAATGGTGAATTCACATAGATGACCCCAGT
GACATTGTTGATTCCAAACTTGTCTTCCTCATTTCCTGCCACAATGGAGTACACGATGCTCTG
ATTAATGGCAGCAGCAGAAATGACACCAACTACAGTCCCTCTGGCCGCAAGCTCACTTACAGG
AGGAGGTCTGTATTCCTCTTGGGTGAAGCGTGGGATCTCTCCAGGATGTAAGACAAGAATTCT
CACCGTGGCACTGCTGGACATCACAGGTTCGCCGTCATCAAAAGCCACAACCACCAGCTTGAA
AATCGTAGTAGGCTCTTCATTAAGATTGACGCGGGTTACTACTCTTCCAGAATCTTCCTCTAC
ATCAAAAATACTGGCTGGGTATGGAAACTGCACGTCGTCCACTCGATACCTCACCCTACTTGC
AGGCATCCCAGGTGGGTCCGCATCTTCAGCATAAACGGTGGTGATTGGTGTCCCCTTGACTGC
ATCTGGAGCCACCATCCCCTTGTAGATGCGTTTGCTAAACACTGGAGGGTAGTCATTCATGTC
CTTCACAATTACCGTGACTGTTGCTATACCAGGTGGCATAGTCCCATAAATGTCAAAGGCCTC
CACCAAGAATGTGATGCTTGCCTCCTGGTCCGGAAAGGCCTCATAATCCAAACTCCTCAGAAG
AGACAATTCTCCAGTGAATGGATGCAGTGCAAAAAGGTGTTTCACTTCTGGGCTTCTGATCCG
ATATGACACATTGGCTCCAAGGTCAACATCCTTGGCCTCTATTTGAAGAAAGGAGGTCCCGGC
TGGCAGATTCTCTTCAACGACAACTGTGTACGTTGAATTGGTAAAAACAGGACTGTTATCATT
TGCATCCATCACTCGGATATTGACCACGACTGGCTCACTTTCTTGCACGCCATCAAACGCTGT

TATCAGAAAGGTGTAGGTTTGCTGTTCCTCCCTGTCCACAGGTTGAAGCAGGGTGAGGTAGCG
GGTGATACCAGTGGGTGTCACAGTGAAGACCGAGGTGTAGTCATTCAGGAAGAGGTGGAGCTC
TGGATCTTTTGTGTCTTCTATGTCTTTGTCCAGAGCTACAATTCTCAGAGGAGTGGTTAAGTT
TAGGCTCTCAGAAATGGTGGCTCCCACTGGGGCGGATTCCAGGATGTATCCTTGATAGCTGGG
CATTGTGAAGTATGGACTCTGATTGTTTTCGTCTAGTATTTCGATGTGCAGACTAGCAAAGGC
AGGAAGTGGGTGGCCATTGTCCTGCTCAGCCTTAATAACCAAATCAAATTTTTGATGGAAGTC
TCTGTTTACTGGCTCCAGGAGAGTGAGTTCTGCAGTCCTGGGATGCATATGGAAGAAGCGGGG
GTAATCCTCAGGGGTGCCGACAAGGATGGAGTAGAGGATGCCAGGTCGATCAGATGGTGGTTG
GATGTTTCGGTCCTGATCAATGGCTTGGATAGGTGGTGTCACCAAAATAGGGTTCAGTTCTTC
CGGAGTCCTCAGTTCAGGAATGGCAGCTTGGTAGGTGAGTGGACGACAGTCACGTGTGTTTGG
CACAAGAACACAAGGCAGAAACATAGGTCCCAGGTCATCTCCATCTAGAACATCTACTGTGAG
GGTGGTGGTGGTTGTTCGCCTCTCATTCAGATTTTGTGCACGGTCATTTGCTTGGATGATGAC
ATAGTAGCGAGTCTTATCCTCATAGTTGAGTCTTTTCCTCAGTACCACGTTGCCAGTCAGCAT
GAGTGGAATTTCAAAGGTGTCGTTGGATGTCGGATCTTCTGGGTTGTACTGAATCACGTATTC
TATCTGTCCATTAGGGCCATCGTCTATGTCTGTAGCTCCATTGTCTCCCGAGAACCCCGTGAA
TATCGTGGTGCCAACTGGAGTGAGCTCATTCACGGTGGCATAGTAGCTTTCATGCTTGAATGT
GGGGGAGTTGTCATTCCGATCTCGCACCACGATGCGTACTTCATGATAGATAACTGTGCCAAC
CTTCTTGTTGACACACTGGACTTGCACCACAATGGAGTGTATGTTCATTGGTGGGTCTCTATC
CAGAACTCTTCCGGTACTGTTCAGGAAAAGCATCTGTTTAACGGGGTCCAGCAACACCCAGTA
GTCCACGTTGTCCTTTAAAGAGAGCTCTATGGTGGGGTCTGGTCCTCCGGCAGTCCCCTTAAT
CAACATGTTATCCACCAGAATTGTACCGTTTCGACTCTCTTCATCAATGGCCACGATAGTAGC
TGGTGGTCCTCCCCTAGCTAGTTTGCAATCCTCGTATTGCCAGTCATCGTCATACTGGCCCCA
GCTGACTACCAAGAGAGAGGCAATGAGGATCCCATGGGGTAAACACTTCCAGACAGCAAACTG
TAGGAACAT (SEQ ID NO: 151)

Mouse mini-PCDH15-CD2-1-V3

AAGGGCTGTGTTGTAACCTTCGGAGTTTGCGCCTGGAGATTTCTTGGGCTCTTCATCCTTCCT
TCTGTCATATTCTGGCACCTGAAAGCCCCAGGGGCCTCCGGAGAGACTCTCACTGGTACTGCT
GCTGCTGCTCAGTTCTGACTCTGACTCCTCACTTTCCACGCCCCTCTCCATGGAGACTGATTC
TGCACTGCCCTCCTCTGGGACATCCTGAGCCTCCAGGTCTGTGGACTCATCCATGGGAGCTGC
TTCGCTTTCTTCTCCTTCCTCTGCCCGTTCTTCCTCCTCTAGTGGGGGCTCTTCTTCCTCTTC
CACCGGGGGCTCCTCTCTCTTACCTTTCACCTCCTGGATTTCCTCGACCACAGGCCTTCTTCT
AGCCAGCACGATGTTTTTTCTTGCTTTCTCTCCCTCTGACTCAGTGGACTCAGACTCCTCTGA
CTCCGGGGTAGAGCTCTCCTCCGCTTCCTCAGATGGGGTCTCCGACTCTGATTCTTCAGTTGT
CTCGGACTCGCTGAACTCGGACTCCGTTTCTGTGTATTCTGTGTAGTCGCTGGACTCCTCCTC
TGACTCCACGGTGCTTTCGGTAGCTTCCTCCTGGTCTAGAGTCAGTTGAAGATAGTCTTTGTC
TTCTTCATCAAGGCGCCTCCTCCACTCCTCGCCCTCAAGGTCAATGCCTCTTTTCTCAGCGAG
ACCTCTGACTTTCTTAAAAATCATCGGGAATATCCTGGCTCTCTTCCACGTTGGGTATGTGGG
CTCAGCCGCTGGTGGCTTCTCAACGGTGACTACCACCTCCTCCTCACTAGGCTCTCTAATTTC
AACTTTGGGTTTTTTAACTTTCTCTGGCTCTACCTCTTCTTCTTCATATTCCTCTTCAGCTTC
ACCAATGACTTCGCCGTATTCCTCCTGTCCAGCAGGTGGCAGCAGTCGACGGCGACTTCCATA
CTGGGGCATCTCATACTTATGCATTGCGCTCTCTCCCAGTTCTTCATAGAGATGTGCTCCTGG
TGGTGGTGGTGGCGGGGGCGGGGGCGGCGCAGGCGCAGCTGGTACAGGAGCTGCAGGCTTGGC
TGCAGGCATAGCAGACTGAATTCTTGCGGTCTTCGTGCACTCAGCCTGGCGTACTTTAAACTG
TCGGTAGCTTACTAAGACGACCAAGATGGCTGGGATGCAACAGAGGATGATGATGAAGGCCAA
GGCCAGCAAGGCCCCTTCTGTGTACCCCAAGCTTTCTCCTCGCTTCTTGATGCTCGTCACTGC

CTCAGGTGTCCGAATCTCCAGAATGCGCCCTCCTTCCCCGTAATACGGCTGGAAGTCTTTATT
GATATCGAGCAGTTTGCCGTCCAGGAACTTAAAAAGCTCATTTCTGTCGATGGCTCTGTTGGT
CTGCGGGTCGATGGCATAGACAGTCAGGTCGCACTTGCTATAGTCTTCTAGGGAGTAGGCGTC
TCCATGGCGACGGGCACCTATGGACTCCACCACAACCTTGGCACCAGGAATTTGCTCCTGAAC
GTAGCGATCCAAAATCTCTGTAAGGTCTTCTATCTTCTTTTCCACTAGTGTAGGGGGCACATT
GGAGACAATGACCTGCATATCCAGTTGATTGACCACGGAGACCAGTACGTCTGCTTTCCCGCT
CAACCCCTTCCCGTAGTCGTCAGTTGCAATCACTTGAAACTTGAAGTAGGATCTTCTCATATT
GTGGAAGAGCATGGCTGTCTTGATGAGACCTGTGTATGTTTCCACCACAAACCCCTCTTTGCC
CTCTTTAATCGGCGGTATGATGAGCCGGTAGGCCATGGCACTGTAATTACCCGTGTCCCTGTC
GGTGGCCTTCACTCTGAGCACAGATGCGAACATCCTTGCGTCTTCAGACACACCTCCAATGTA
GAATTTCTTCTGGAACACTGGGGGGTGATCGTTTTCATCCTGAATCTCAATGTACACCTTAGC
TGTATTGCTTTTTGAAGGGACTCGGAGATTGGCAAGGACCACTTCCAGAGAATCTGCTTGTAC
CCGGAGCACATAGCTGGTCCTTGTCTCGTAATCCAATGGTGAATTCACATAGATGACCCCAGT
GACATTGTTGATTCCAAACTTGTCTTCCTCATTTCCTGCCACAATGGAGTACACGATGCTCTG
ATTAATGGCAGCAGCAGAAATGACACCAACTACAGTCCCTCTGGCCGCAAGCTCACTTACAGG
AGGAGGTCTGTATTCCTCTTGGGTGAAGCGTGGGATCTCTCCAGGATGTAAGACAAGAATTCT
CACCGTGGCACTGCTGGACATCACAGGTTCGCCGTCATCAAAAGCCACAACCACCAGCTTGAA
AATCGTAGTAGGCTCTTCATTAAGATTGACGCGGGTTACTACTCTTCCAGAATCTTCCTCTAC
ATCAAAAATACTGGCTGGGTATGGAAACTGCACGTCGTCCACTCGATACCTCACCCTACTTGC
AGGCATCCCAGGTGGGTCCGCATCTTCAGCATAAACGGTGGTGATTGGTGTCCCCTTGACTGC
ATCTGGAGCCACCATCCCCTTGTAGATGCGTTTGCTAAACACTGGAGGGTAGTCATTCATGTC
CTTCACAATTACCGTGACTGTTGCTATACCAGGTGGCATAGTCCCATAAATGTCAAAGGCCTC
CACCAAGAATGTGATGCTTGCCTCCTGGTCCGGAAAGGCCTCATAATCCAAACTCCTCAGAAG
AGACAATTCTCCAGTGAATGGATGCAGTGCAAAAAGGTGTTTCACTTCTGGGCTTCTGATCCG
ATATGACACATTGGCTCCAAGGTCAACATCCTTGGCCTCTATTTGAAGAAAGGAGGTCCCGGC
TGGCAGATTCTCTTCAACGACAACTGTGTACGTTGAATTGGTAAAAACAGGACTCTGATTGTT
TTCGTCTAGTATTTCGATGTGCAGACTAGCAAAGGCAGGAAGTGGGTGGCCATTGTCCTGCTC
AGCCTTAATAACCAAATCAAATTTTTGATGGAAGTCTCTGTTTACTGGCTCCAGGAGAGTGAG
TTCTGCAGTCCTGGGATGCATATGGAAGAAGCGGGGGTAATCCTCAGGGGTGCCGACAAGGAT
GGAGTAGAGGATGCCAGGTCGATCAGATGGTGGTTGGATGTTTCGGTCCTGATCAATGGCTTG
GATAGGTGGTGTCACCAAAATAGGGTTCAGTTCTTCCGGAGTCCTCAGTTCAGGAATGGCAGC
TTGGTAGGTGAGTGGACGACAGTCACGTGTGTTTGGCACAAGAACACAAGGCAGAAACATAGG
TCCCAGGTCATCTCCATCTAGAACATCTACTGTGAGGGTGGTGGTGGTTGTTCGCCTCTCATT
CAGATTTTGTGCACGGTCATTTGCTTGGATGATGACATAGTAGCGAGTCTTATCCTCATAGTT
GAGTCTTTTCCTCAGTACCACGTTGCCAGTCAGCATGAGTGGAATTTCAAAGGTGTCGTTGGA
TGTCGGATCTTCTGGGTTGTACTGAATCACGTATTCTATCTGTCCATTAGGGCCATCGTCTAT
GTCTGTAGCTCCATTGTCTCCCGAGAACCCCGTGAATATCGTGGTGCCAACTGGAGTGAGCTC
ATTCACGGTGGCATAGTAGCTTTCATGCTTGAATGTGGGGGAGTTGTCATTCCGATCTCGCAC
CACGATGCGTACTTCATGATAGATAACTGTGCCAACCTTCTTGTTGACACACTGGACTTGCAC
CACAATGGAGTGTATGTTCATTGGTGGGTCTCTATCCAGAACTCTTCCGGTACTGTTCAGGAA
AAGCATCTGTTTAACGGGGTCCAGCAACACCCAGTAGTCCACGTTGTCCTTTAAAGAGAGCTC
TATGGTGGGGTCTGGTCCTCCGGCAGTCCCCTTAATCAACATGTTATCCACCAGAATTGTACC
GTTTCGACTCTCTTCATCAATGGCCACGATAGTAGCTGGTGGTCCTCCCCTAGCTAGTTTGCA
ATCCTCGTATTGCCAGTCATCGTCATACTGGCCCCAGCTGACTACCAAGAGAGAGGCAATGAG
GATCCCATGGGGTAAACACTTCCAGACAGCAAACTGTAGGAACAT (SEQ ID NO: 63)

Mouse mini-PCDH15-CD2-1-V4

AAGGGCTGTGTTGTAACCTTCGGAGTTTGCGCCTGGAGATTTCTTGGGCTCTTCATCCTTCCT
TCTGTCATATTCTGGCACCTGAAAGCCCCAGGGGCCTCCGGAGAGACTCTCACTGGTACTGCT
GCTGCTGCTCAGTTCTGACTCTGACTCCTCACTTTCCACGCCCCTCTCCATGGAGACTGATTC
TGCACTGCCCTCCTCTGGGACATCCTGAGCCTCCAGGTCTGTGGACTCATCCATGGGAGCTGC
TTCGCTTTCTTCTCCTTCCTCTGCCCGTTCTTCCTCCTCTAGTGGGGGCTCTTCTTCCTCTTC
CACCGGGGGCTCCTCTCTCTTACCTTTCACCTCCTGGATTTCCTCGACCACAGGCCTTCTTCT
AGCCAGCACGATGTTTTTTCTTGCTTTCTCTCCCTCTGACTCAGTGGACTCAGACTCCTCTGA
CTCCGGGGTAGAGCTCTCCTCCGCTTCCTCAGATGGGGTCTCCGACTCTGATTCTTCAGTTGT
CTCGGACTCGCTGAACTCGGACTCCGTTTCTGTGTATTCTGTGTAGTCGCTGGACTCCTCCTC
TGACTCCACGGTGCTTTCGGTAGCTTCCTCCTGGTCTAGAGTCAGTTGAAGATAGTCTTTGTC
TTCTTCATCAAGGCGCCTCCTCCACTCCTCGCCCTCAAGGTCAATGCCTCTTTTCTCAGCGAG
ACCTCTGACTTTCTTAAAAATCATCGGGAATATCCTGGCTCTCTTCCACGTTGGGTATGTGGG
CTCAGCCGCTGGTGGCTTCTCAACGGTGACTACCACCTCCTCCTCACTAGGCTCTCTAATTTC
AACTTTGGGTTTTTTAACTTTCTCTGGCTCTACCTCTTCTTCTTCATATTCCTCTTCAGCTTC
ACCAATGACTTCGCCGTATTCCTCCTGTCCAGCAGGTGGCAGCAGTCGACGGCGACTTCCATA
CTGGGGCATCTCATACTTATGCATTGCGCTCTCTCCCAGTTCTTCATAGAGATGTGCTCCTGG
TGGTGGTGGTGGCGGGGGCGGGGGCGGCGCAGGCGCAGCTGGTACAGGAGCTGCAGGCTTGGC
TGCAGGCATAGCAGACTGAATTCTTGCGGTCTTCGTGCACTCAGCCTGGCGTACTTTAAACTG
TCGGTAGCTTACTAAGACGACCAAGATGGCTGGGATGCAACAGAGGATGATGATGAAGGCCAA
GGCCAGCAAGGCCCCTTCTGTGTACCCCAAGCTTTCTCCTCGCTTCTTGATGCTCGTCACTGC
CTCAGGTGTCCGAATCTCCAGAATGCGCCCTCCTTCCCCGTAATACGGCTGGAAGTCTTTATT
GATATCGAGCAGTTTGCCGTCCAGGAACTTAAAAAGCTCATTTCTGTCGATGGCTCTGTTGGT
CTGCGGGTCGATGGCATAGACAGTCAGGTCGCACTTGCTATAGTCTTCTAGGGAGTAGGCGTC
TCCATGGCGACGGGCACCTATGGACTCCACCACAACCTTGGCACCAGGAATTTGCTCCTGAAC
GTAGCGATCCAAAATCTCTGTAAGGTCTTCTATCTTCTTTTCCACTAGTGTAGGGGGCACATT
GGAGACAATGACCTGCATATCCAGTTGATTGACCACGGAGACCAGTACGTCTGCTTTCCCGCT
CAACCCCTTCCCGTAGTCGTCAGTTGCAATCACTTGAAACTTGAAGTAGGATCTTCTCATATT
GTGGAAGAGCATGGCTGTCTTGATGAGACCTGTGTATGTTTCCACCACAAACCCCTCTTTGCC
CTCTTTAATCGGCGGTATGATGAGCCGGTAGGCCATGGCACTGTAATTACCCGTGTCCCTGTC
GGTGGCCTTCACTCTGAGCACAGATGCGAACATCCTTGCGTCTTCAGACACACCTCCAATGTA
GAATTTCTTCTGGAACACTGGGGGGTGATCGTTTTCATCCTGAATCTCAATGTACACCTTAGC
TGTATTGCTTTTTGAAGGGACTCGGAGATTGGCAAGGACCACTTCCAGAGAATCTGCTTGTAC
CCGGAGCACATAGCTGGTCCTTGTCTCGTAATCCAATGGTGAATTCACATAGATGACCCCAGT
GACATTGTTGATTCCAAACTTGTCTTCCTCATTTCCTGCCACAATGGAGTACACGATGCTCTG
ATTAATGGCAGCAGCAGAAATGACACCAACTACAGTCCCTCTGGCCGCAAGCTCACTTACAGG
AGGAGGTCTGTATTCCTCTTGGGTGAAGCGTGGGATCTCTCCAGGATGTAAGACAAGAATTCT
CACCGTGGCACTGCTGGACATCACAGGTTCGCCGTCATCAAAAGCCACAACCACCAGCTTGAA
AATCGTAGTAGGCTCTTCATTAAGATTGACGCGGGTTACTACTCTTCCAGAATCTTCCTCTAC
ATCAAAAATACTGGCTGGGTATGGAAACTGCACGTCGTCCACTCGATACCTCACCCTACTTGC
AGGCATCCCAGGTGGGTCCGCATCTTCAGCATAAACGGTGGTGATTGGTGTCCCCTTGACTGC
ATCTGGAGCCACCATCCCCTTGTAGATGCGTTTGCTAAACACTGGAGGCTGATTGTTTTCGTC
TAGTATTTCGATGTGCAGACTAGCAAAGGCAGGAAGTGGGTGGCCATTGTCCTGCTCAGCCTT
AATAACCAAATCAAATTTTTGATGGAAGTCTCTGTTTACTGGCTCCAGGAGAGTGAGTTCTGC
AGTCCTGGGATGCATATGGAAGAAGCGGGGGTAATCCTCAGGGGTGCCGACAAGGATGGAGTA
GAGGATGCCAGGTCGATCAGATGGTGGTTGGATGTTTCGGTCCTGATCAATGGCTTGGATAGG
TGGTGTCACCAAAATAGGGTTCAGTTCTTCCGGAGTCCTCAGTTCAGGAATGGCAGCTTGGTA
GGTGAGTGGACGACAGTCACGTGTGTTTGGCACAAGAACACAAGGCAGAAACATAGGTCCCA

GGTCATCTCCATCTAGAACATCTACTGTGAGGGTGGTGGTGGTTGTTCGCCTCTCATTCAGAT
TTTGTGCACGGTCATTTGCTTGGATGATGACATAGTAGCGAGTCTTATCCTCATAGTTGAGTC
TTTTCCTCAGTACCACGTTGCCAGTCAGCATGAGTGGAATTTCAAAGGTGTCGTTGGATGTCG
GATCTTCTGGGTTGTACTGAATCACGTATTCTATCTGTCCATTAGGGCCATCGTCTATGTCTG
TAGCTCCATTGTCTCCCGAGAACCCCGTGAATATCGTGGTGCCAACTGGAGTGAGCTCATTCA
CGGTGGCATAGTAGCTTTCATGCTTGAATGTGGGGGAGTTGTCATTCCGATCTCGCACCACGA
TGCGTACTTCATGATAGATAACTGTGCCAACCTTCTTGTTGACACACTGGACTTGCACCACAA
TGGAGTGTATGTTCATTGGTGGGTCTCTATCCAGAACTCTTCCGGTACTGTTCAGGAAAAGCA
TCTGTTTAACGGGGTCCAGCAACACCCAGTAGTCCACGTTGTCCTTTAAAGAGAGCTCTATGG
TGGGGTCTGGTCCTCCGGCAGTCCCCTTAATCAACATGTTATCCACCAGAATTGTACCGTTTC
GACTCTCTTCATCAATGGCCACGATAGTAGCTGGTGGTCCTCCCCTAGCTAGTTTGCAATCCT
CGTATTGCCAGTCATCGTCATACTGGCCCCAGCTGACTACCAAGAGAGAGGCAATGAGGATCC
CATGGGGTAAACACTTCCAGACAGCAAACTGTAGGAACAT (SEQ ID NO: 64)

Mouse mini-PCDH15-CD2-1-V5

AAGGGCTGTGTTGTAACCTTCGGAGTTTGCGCCTGGAGATTTCTTGGGCTCTTCATCCTTCCT
TCTGTCATATTCTGGCACCTGAAAGCCCCAGGGGCCTCCGGAGAGACTCTCACTGGTACTGCT
GCTGCTGCTCAGTTCTGACTCTGACTCCTCACTTTCCACGCCCCTCTCCATGGAGACTGATTC
TGCACTGCCCTCCTCTGGGACATCCTGAGCCTCCAGGTCTGTGGACTCATCCATGGGAGCTGC
TTCGCTTTCTTCTCCTTCCTCTGCCCGTTCTTCCTCCTCTAGTGGGGGCTCTTCTTCCTCTTC
CACCGGGGGCTCCTCTCTCTTACCTTTCACCTCCTGGATTTCCTCGACCACAGGCCTTCTTCT
AGCCAGCACGATGTTTTTTCTTGCTTTCTCTCCCTCTGACTCAGTGGACTCAGACTCCTCTGA
CTCCGGGGTAGAGCTCTCCTCCGCTTCCTCAGATGGGGTCTCCGACTCTGATTCTTCAGTTGT
CTCGGACTCGCTGAACTCGGACTCCGTTTCTGTGTATTCTGTGTAGTCGCTGGACTCCTCCTC
TGACTCCACGGTGCTTTCGGTAGCTTCCTCCTGGTCTAGAGTCAGTTGAAGATAGTCTTTGTC
TTCTTCATCAAGGCGCCTCCTCCACTCCTCGCCCTCAAGGTCAATGCCTCTTTTCTCAGCGAG
ACCTCTGACTTTCTTAAAAATCATCGGGAATATCCTGGCTCTCTTCCACGTTGGGTATGTGGG
CTCAGCCGCTGGTGGCTTCTCAACGGTGACTACCACCTCCTCCTCACTAGGCTCTCTAATTTC
AACTTTGGGTTTTTTAACTTTCTCTGGCTCTACCTCTTCTTCTTCATATTCCTCTTCAGCTTC
ACCAATGACTTCGCCGTATTCCTCCTGTCCAGCAGGTGGCAGCAGTCGACGGCGACTTCCATA
CTGGGGCATCTCATACTTATGCATTGCGCTCTCTCCCAGTTCTTCATAGAGATGTGCTCCTGG
TGGTGGTGGTGGCGGGGGCGGGGGCGGCGCAGGCGCAGCTGGTACAGGAGCTGCAGGCTTGGC
TGCAGGCATAGCAGACTGAATTCTTGCGGTCTTCGTGCACTCAGCCTGGCGTACTTTAAACTG
TCGGTAGCTTACTAAGACGACCAAGATGGCTGGGATGCAACAGAGGATGATGATGAAGGCCAA
GGCCAGCAAGGCCCCTTCTGTGTACCCCAAGCTTTCTCCTCGCTTCTTGATGCTCGTCACTGC
CTCAGGTGTCCGAATCTCCAGAATGCGCCCTCCTTCCCCGTAATACGGCTGGAAGTCTTTATT
GATATCGAGCAGTTTGCCGTCCAGGAACTTAAAAAGCTCATTTCTGTCGATGGCTCTGTTGGT
CTGCGGGTCGATGGCATAGACAGTCAGGTCGCACTTGCTATAGTCTTCTAGGGAGTAGGCGTC
TCCATGGCGACGGGCACCTATGGACTCCACCACAACCTTGGCACCAGGAATTTGCTCCTGAAC
GTAGCGATCCAAAATCTCTGTAAGGTCTTCTATCTTCTTTTCCACTAGTGTAGGGGGCACATT
GGAGACAATGACCTGCATATCCAGTTGATTGACCACGGAGACCAGTACGTCTGCTTTCCCGCT
CAACCCCTTCCCGTAGTCGTCAGTTGCAATCACTTGAAACTTGAAGTAGGATCTTCTCATATT
GTGGAAGAGCATGGCTGTCTTGATGAGACCTGTGTATGTTTCCACCACAAACCCCTCTTTGCC
CTCTTTAATCGGCGGTATGATGAGCCGGTAGGCCATGGCACTGTAATTACCCGTGTCCCTGTC
GGTGGCCTTCACTCTGAGCACAGATGCGAACATCCTTGCGTCTTCAGACACACCTCCAATGTA
GAATTTCTTCTGGAACACTGGGGGGTTATCATCAATGTCCAACACCTTGATGTACAGTGTCAG

AGTTGAATGTCGAGGGTGGACTGCTCCATCTGTTGCCACGACAACCAGTTCATAGTGGTCCCT
GGCTTCCCTGTTCAGCTTCACGGCTGTGTAAATGCTCCCGTTGGATGTGATGCGGAAGAGGTT
GTTGAAGTTCCCCAGGCTGTAGTGAACTTGGCCGTTTATCCCAGCATCTGGGTCTGTTGCCCG
GACTTGACCCACAAAGGCATTGGCTTCTTCCTCCACCACAGAGAGGTTCCTGGGCAGATAGGG
ATCGAACACGGGAGCGTTGTCATTGACGTCCGTCACCACTATGTTCACAGTGGCAGTTGAGGT
TCCATCCGGTCTGCCATCTGAGGCTGTGACGATGAGGATGTAGCGGTCTGTGCTCTCGCGGTC
TAGAGCCTTCCCTAGGCTGAGAATCCCTGTGGTTTCTGAAAGATTAAAAACTCTCTGAGGGTC
TCCATTCTCGATGGCATATGTGATTGGATCTCCCTCTCGATCAGTTGCCTGTAGATTTAATAA
AATAGCACCGATCCTCATGGCCTCGCTGACTTCCAGACTGTACATCAGCTGCGGGAAGCGGGG
AGGGCTCTGGTTGTTAGGAGGAAGCACCTCGATGTACACTGTGCAGATGGAGTGCCTTCTTTC
TGCAGGCGGGGCGTTGTCCGAAGCCTGCACTGTGAGCGCATACGTCTGTCCCACGATCAGCTC
CACGCCTGGTGCAATGCTCACCAGCCCTGTGGTCTTGTTGATCACGAAGTCTCCCTTGCCCCC
CACCAGTATTTCATAGGAGATCTCCCCATTAGAGCCTTCATCAGCATCTACCGCTGTCAGCTG
AATGACGCTGTCCCCAGGACTCATGTCTGTGTAAACATAGACATCATAGGAGATTTCAGGGAA
GGTGGGCGTCTGATTGTTTTCGTCTAGTATTTCGATGTGCAGACTAGCAAAGGCAGGAAGTGG
GTGGCCATTGTCCTGCTCAGCCTTAATAACCAAATCAAATTTTTGATGGAAGTCTCTGTTTAC
TGGCTCCAGGAGAGTGAGTTCTGCAGTCCTGGGATGCATATGGAAGAAGCGGGGGTAATCCTC
AGGGGTGCCGACAAGGATGGAGTAGAGGATGCCAGGTCGATCAGATGGTGGTTGGATGTTTCG
GTCCTGATCAATGGCTTGGATAGGTGGTGTCACCAAAATAGGGTTCAGTTCTTCCGGAGTCCT
CAGTTCAGGAATGGCAGCTTGGTAGGTGAGTGGACGACAGTCACGTGTGTTTGGCACAAGAAC
ACAAGGCAGAAACATAGGTCCCAGGTCATCTCCATCTAGAACATCTACTGTGAGGGTGGTGGT
GGTTGTTCGCCTCTCATTCAGATTTTGTGCACGGTCATTTGCTTGGATGATGACATAGTAGCG
AGTCTTATCCTCATAGTTGAGTCTTTTCCTCAGTACCACGTTGCCAGTCAGCATGAGTGGAAT
TTCAAAGGTGTCGTTGGATGTCGGATCTTCTGGGTTGTACTGAATCACGTATTCTATCTGTCC
ATTAGGGCCATCGTCTATGTCTGTAGCTCCATTGTCTCCCGAGAACCCCGTGAATATCGTGGT
GCCAACTGGAGTGAGCTCATTCACGGTGGCATAGTAGCTTTCATGCTTGAATGTGGGGGAGTT
GTCATTCCGATCTCGCACCACGATGCGTACTTCATGATAGATAACTGTGCCAACCTTCTTGTT
GACACACTGGACTTGCACCACAATGGAGTGTATGTTCATTGGTGGGTCTCTATCCAGAACTCT
TCCGGTACTGTTCAGGAAAAGCATCTGTTTAACGGGGTCCAGCAACACCCAGTAGTCCACGTT
GTCCTTTAAAGAGAGCTCTATGGTGGGGTCTGGTCCTCCGGCAGTCCCCTTAATCAACATGTT
ATCCACCAGAATTGTACCGTTTCGACTCTCTTCATCAATGGCCACGATAGTAGCTGGTGGTCC
TCCCCTAGCTAGTTTGCAATCCTCGTATTGCCAGTCATCGTCATACTGGCCCCAGCTGACTAC
CAAGAGAGAGGCAATGAGGATCCCATGGGGTAAACACTTCCAGACAGCAAACTGTAGGAACAT
(SEQ ID NO: 65)

Mouse mini-PCDH15-CD2-1-V6:

AAGGGCTGTGTTGTAACCTTCGGAGTTTGCGCCTGGAGATTTCTTGGGCTCTTCATCCTTCCT
TCTGTCATATTCTGGCACCTGAAAGCCCCAGGGGCCTCCGGAGAGACTCTCACTGGTACTGCT
GCTGCTGCTCAGTTCTGACTCTGACTCCTCACTTTCCACGCCCCTCTCCATGGAGACTGATTC
TGCACTGCCCTCCTCTGGGACATCCTGAGCCTCCAGGTCTGTGGACTCATCCATGGGAGCTGC
TTCGCTTTCTTCTCCTTCCTCTGCCCGTTCTTCCTCCTCTAGTGGGGGCTCTTCTTCCTCTTC
CACCGGGGGCTCCTCTCTCTTACCTTTCACCTCCTGGATTTCCTCGACCACAGGCCTTCTTCT
AGCCAGCACGATGTTTTTTCTTGCTTTCTCTCCCTCTGACTCAGTGGACTCAGACTCCTCTGA
CTCCGGGGTAGAGCTCTCCTCCGCTTCCTCAGATGGGGTCTCCGACTCTGATTCTTCAGTTGT
CTCGGACTCGCTGAACTCGGACTCCGTTTCTGTGTATTCTGTGTAGTCGCTGGACTCCTCCTC
TGACTCCACGGTGCTTTCGGTAGCTTCCTCCTGGTCTAGAGTCAGTTGAAGATAGTCTTTGTC

TTCTTCATCAAGGCGCCTCCTCCACTCCTCGCCCTCAAGGTCAATGCCTCTTTTCTCAGCGAG
ACCTCTGACTTTCTTAAAAATCATCGGGAATATCCTGGCTCTCTTCCACGTTGGGTATGTGGG
CTCAGCCGCTGGTGGCTTCTCAACGGTGACTACCACCTCCTCCTCACTAGGCTCTCTAATTTC
AACTTTGGGTTTTTTAACTTTCTCTGGCTCTACCTCTTCTTCTTCATATTCCTCTTCAGCT
TCACCAATGACTTCGCCGTATTCCTCCTGTCCAGCAGGTGGCAGCAGTCGACGGCGACTTCCA
TACTGGGGCATCTCATACTTATGCATTGCGCTCTCTCCCAGTTCTTCATAGAGATGTGCTCCT
GGTGGTGGTGGTGGCGGGGGCGGGGGCGGCGCAGGCGCAGCTGGTACAGGAGCTGCAGGCTTG
GCTGCAGGCATAGCAGACTGAATTCTTGCGGTCTTCGTGCACTCAGCCTGGCGTACTTTAAAC
TGTCGGTAGCTTACTAAGACGACCAAGATGGCTGGGATGCAACAGAGGATGATGATGAAGGCC
AAGGCCAGCAAGGCCCCTTCTGTGTACCCCAAGCTTTCTCCTCGCTTCTTGATGCTCGTCACT
GCCTCAGGTGTCCGAATCTCCAGAATGCGCCCTCCTTCCCCGTAATACGGCTGGAAGTCTTTA
TTGATATCGAGCAGTTTGCCGTCCAGGAACTTAAAAAGCTCATTTCTGTCGATGGCTCTGTTG
GTCTGCGGGTCGATGGCATAGACAGTCAGGTCGCACTTGCTATAGTCTTCTAGGGAGTAGGCG
TCTCCATGGCGACGGGCACCTATGGACTCCACCACAACCTTGGCACCAGGAATTTGCTCCTGA
ACGTAGCGATCCAAAATCTCTGTAAGGTCTTCTATCTTCTTTTCCACTAGTGTAGGGGGCACA
TTGGAGACAATGACCTGCATATCCAGTTGATTGACCACGGAGACCAGTACGTCTGCTTTCCCG
CTCAACCCCTTCCCGTAGTCGTCAGTTGCAATCACTTGAAACTTGAAGTAGGATCTTCTCATA
TTGTGGAAGAGCATGGCTGTCTTGATGAGACCTGTGTATGTTTCCACCACAAACCCCTCTT
TGCCCTCTTTAATCGGCGGTATGATGAGCCGGTAGGCCATGGCACTGTAATTACCCGTGTCCC
TGTCGGTGGCCTTCACTCTGAGCACAGATGCGAACATCCTTGCGTCTTCAGACACACCTCCAA
TGTAGAATTTCTTCTGGAACACTGGGGGGTAGTCATTCATGTCCTTCACAATTACCGTGACTG
TTGCTATACCAGGTGGCATAGTCCCATAAATGTCAAAGGCCTCCACCAAGAATGTGATGCTTG
CCTCCTGGTCCGGAAAGGCCTCATAATCCAAACTCCTCAGAAGAGACAATTCTCCAGTGAATG
GATGCAGTGCAAAAAGGTGTTTCACTTCTGGGCTTCTGATCCGATATGACACATTGGCTCCAA
GGTCAACATCCTTGGCCTCTATTTGAAGAAAGGAGGTCCCGGCTGGCAGATTCTCTTCAACGA
CAACTGTGTACGTTGAATTGGTAAAAACAGGACTGTTATCATCAATGTCCAACACCTTGATGT
ACAGTGTCAGAGTTGAATGTCGAGGGTGGACTGCTCCATCTGTTGCCACGACAACCAGTTCAT
AGTGGTCCCTGGCTTCCCTGTTCAGCTTCACGGCTGTGTAAATGCTCCCGTTGGATGTGATGC
GGAAGAGGTTGTTGAAGTTCCCCAGGCTGTAGTGAACTTGGCCGTTTATCCCAGCATCTGGGT
CTGTTGCCCGGACTTGACCCACAAAGGCATTGGCTTCTTCCTCCACCACAGAGAGGTTCCTGG
GCAGATAGGGATCGAACACGGGAGCGTTATCATTTGCATCCATCACTCGGATATTGACCACGA
CTGGCTCACTTTCTTGCACGCCATCAAACGCTGTTATCAGAAAGGTGTAGGTTTGCTGTTCCT
CCCTGTCCACAGGTTGAAGCAGGGTGAGGTAGCGGGTGATACCAGTGGGTGTCACAGTGAAGA
CCGAGGTGTAGTCATTCAGGAAGAGGTGGAGCTCTGGATCTTTTGTGTCTTCTATGTCTTTGT
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GGGCGGATTCCAGGATGTATCCTTGATAGCTGGGCATTGTGAAGTATGGACTCTGATTGTTTT
CGTCTAGTATTTCGATGTGCAGACTAGCAAAGGCAGGAAGTGGGTGGCCATTGTCCTGCTCAG
CCTTAATAACCAAATCAAATTTTTGATGGAAGTCTCTGTTTACTGGCTCCAGGAGAGTGAGTT
CTGCAGTCCTGGGATGCATATGGAAGAAGCGGGGGTAATCCTCAGGGGTGCCGACAAGGATGG
AGTAGAGGATGCCAGGTCGATCAGATGGTGGTTGGATGTTTCGGTCCTGATCAATGGCTTGGA
TAGGTGGTGTCACCAAAATAGGGTTCAGTTCTTCCGGAGTCCTCAGTTCAGGAATGGCAGCTT
GGTAGGTGAGTGGACGACAGTCACGTGTGTTTGGCACAAGAACACAAGGCAGAAACATAGGTC
CCAGGTCATCTCCATCTAGAACATCTACTGTGAGGGTGGTGGTGGTTGTTCGCCTCTCATTCA
GATTTTGTGCACGGTCATTTGCTTGGATGATGACATAGTAGCGAGTCTTATCCTCATAGTTGA
GTCTTTTCCTCAGTACCACGTTGCCAGTCAGCATGAGTGGAATTTCAAAGGTGTCGTTGGATG
TCGGATCTTCTGGGTTGTACTGAATCACGTATTCTATCTGTCCATTAGGGCCATCGTCTATGT
CTGTAGCTCCATTGTCTCCCGAGAACCCCGTGAATATCGTGGTGCCAACTGGAGTGAGCTCAT

TCACGGTGGCATAGTAGCTTTCATGCTTGAATGTGGGGGAGTTGTCATTCCGATCTCGCACCA
CGATGCGTACTTCATGATAGATAACTGTGCCAACCTTCTTGTTGACACACTGGACTTGCACCA
CAATGGAGTGTATGTTCATTGGTGGGTCTCTATCCAGAACTCTTCCGGTACTGTTCAGGAAAA
GCATCTGTTTAACGGGGTCCAGCAACACCCAGTAGTCCACGTTGTCCTTTAAAGAGAGCTCTA
TGGTGGGGTCTGGTCCTCCGGCAGTCCCCTTAATCAACATGTTATCCACCAGAATTGTACCGT
TTCGACTCTCTTCATCAATGGCCACGATAGTAGCTGGTGGTCCTCCCCTAGCTAGTTTGCAAT
CCTCGTATTGCCAGTCATCGTCATACTGGCCCCAGCTGACTACCAAGAGAGAGGCAATGAGGA
TCCCATGGGGTAAACACTTCCAGACAGCAAACTGTAGGAACAT (SEQ ID NO: 66)

Mouse mini-PCDH15-CD2-1-V7:

AAGGGCTGTGTTGTAACCTTCGGAGTTTGCGCCTGGAGATTTCTTGGGCTCTTCATCCTTCCT
TCTGTCATATTCTGGCACCTGAAAGCCCCAGGGGCCTCCGGAGAGACTCTCACTGGTACTGCT
GCTGCTGCTCAGTTCTGACTCTGACTCCTCACTTTCCACGCCCCTCTCCATGGAGACTGATTC
TGCACTGCCCTCCTCTGGGACATCCTGAGCCTCCAGGTCTGTGGACTCATCCATGGGAGCTGC
TTCGCTTTCTTCTCCTTCCTCTGCCCGTTCTTCCTCCTCTAGTGGGGGCTCTTCTTCCTCTTC
CACCGGGGGCTCCTCTCTCTTACCTTTCACCTCCTGGATTTCCTCGACCACAGGCCTTCTTCT
AGCCAGCACGATGTTTTTTCTTGCTTTCTCTCCCTCTGACTCAGTGGACTCAGACTCCTCTGA
CTCCGGGGTAGAGCTCTCCTCCGCTTCCTCAGATGGGGTCTCCGACTCTGATTCTTCAGTTGT
CTCGGACTCGCTGAACTCGGACTCCGTTTCTGTGTATTCTGTGTAGTCGCTGGACTCCTCCTC
TGACTCCACGGTGCTTTCGGTAGCTTCCTCCTGGTCTAGAGTCAGTTGAAGATAGTCTTTGTC
TTCTTCATCAAGGCGCCTCCTCCACTCCTCGCCCTCAAGGTCAATGCCTCTTTTCTCAGCGAG
ACCTCTGACTTTCTTAAAAATCATCGGGAATATCCTGGCTCTCTTCCACGTTGGGTATGTGGG
CTCAGCCGCTGGTGGCTTCTCAACGGTGACTACCACCTCCTCCTCACTAGGCTCTCTAATTTC
AACTTTGGGTTTTTTAACTTTCTCTGGCTCTACCTCTTCTTCTTCATATTCCTCTTCAGCTTC
ACCAATGACTTCGCCGTATTCCTCCTGTCCAGCAGGTGGCAGCAGTCGACGGCGACTTCCATA
CTGGGGCATCTCATACTTATGCATTGCGCTCTCTCCCAGTTCTTCATAGAGATGTGCTCCTGG
TGGTGGTGGTGGCGGGGGCGGGGGCGGCGCAGGCGCAGCTGGTACAGGAGCTGCAGGCTTGGC
TGCAGGCATAGCAGACTGAATTCTTGCGGTCTTCGTGCACTCAGCCTGGCGTACTTTAAACTG
TCGGTAGCTTACTAAGACGACCAAGATGGCTGGGATGCAACAGAGGATGATGATGAAGGCCAA
GGCCAGCAAGGCCCCTTCTGTGTACCCCAAGCTTTCTCCTCGCTTCTTGATGCTCGTCACTGC
CTCAGGTGTCCGAATCTCCAGAATGCGCCCTCCTTCCCCGTAATACGGCTGGAAGTCTTTATT
GATATCGAGCAGTTTGCCGTCCAGGAACTTAAAAAGCTCATTTCTGTCGATGGCTCTGTTGGT
CTGCGGGTCGATGGCATAGACAGTCAGGTCGCACTTGCTATAGTCTTCTAGGGAGTAGGCGTC
TCCATGGCGACGGGCACCTATGGACTCCACCACAACCTTGGCACCAGGAATTTGCTCCTGAAC
GTAGCGATCCAAAATCTCTGTAAGGTCTTCTATCTTCTTTTCCACTAGTGTAGGGGGCACATT
GGAGACAATGACCTGCATATCCAGTTGATTGACCACGGAGACCAGTACGTCTGCTTTCCCGCT
CAACCCCTTCCCGTAGTCGTCAGTTGCAATCACTTGAAACTTGAAGTAGGATCTTCTCATATT
GTGGAAGAGCATGGCTGTCTTGATGAGACCTGTGTATGTTTCCACCACAAACCCCTCTTTGCC
CTCTTTAATCGGCGGTATGATGAGCCGGTAGGCCATGGCACTGTAATTACCCGTGTCCCTGTC
GGTGGCCTTCACTCTGAGCACAGATGCGAACATCCTTGCGTCTTCAGACACACCTCCAATGTA
GAATTTCTTCTGGAACACTGGGGGGTAGTCATTCATGTCCTTCACAATTACCGTGACTGTTGC
TATACCAGGTGGCATAGTCCCATAAATGTCAAAGGCCTCCACCAAGAATGTGATGCTTGCCTC
CTGGTCCGGAAAGGCCTCATAATCCAAACTCCTCAGAAGAGACAATTCTCCAGTGAATGGATG
CAGTGCAAAAAGGTGTTTCACTTCTGGGCTTCTGATCCGATATGACACATTGGCTCCAAGGTC
AACATCCTTGGCCTCTATTTGAAGAAAGGAGGTCCCGGCTGGCAGATTCTCTTCAACGACAAC
TGTGTACGTTGAATTGGTAAAAACAGGACTGTTATCATCAATGTCCAACACCTTGATGTACAG

TGTCAGAGTTGAATGTCGAGGGTGGACTGCTCCATCTGTTGCCACGACAACCAGTTCATAGTG
GTCCCTGGCTTCCCTGTTCAGCTTCACGGCTGTGTAAATGCTCCCGTTGGATGTGATGCGGAA
GAGGTTGTTGAAGTTCCCCAGGCTGTAGTGAACTTGGCCGTTTATCCCAGCATCTGGGTCTGT
TGCCCGGACTTGACCCACAAAGGCATTGGCTTCTTCCTCCACCACAGAGAGGTTCCTGGGCAG
ATAGGGATCGAACACGGGAGCCTGATTGTTTTCGTCTAGTATTTCGATGTGCAGACTAGCAAA
GGCAGGAAGTGGGTGGCCATTGTCCTGCTCAGCCTTAATAACCAAATCAAATTTTTGATGGAA
GTCTCTGTTTACTGGCTCCAGGAGAGTGAGTTCTGCAGTCCTGGGATGCATATGGAAGAAGCG
GGGGTAATCCTCAGGGGTGCCGACAAGGATGGAGTAGAGGATGCCAGGTCGATCAGATGGTGG
TTGGATGTTTCGGTCCTGATCAATGGCTTGGATAGGTGGTGTCACCAAAATAGGGTTCAGTTC
TTCCGGAGTCCTCAGTTCAGGAATGGCAGCTTGGTAGGTGAGTGGACGACAGTCACGTGTGTT
TGGCACAAGAACACAAGGCAGAAACATAGGTCCCAGGTCATCTCCATCTAGAACATCTACTG
TGAGGGTGGTGGTGGTTGTTCGCCTCTCATTCAGATTTTGTGCACGGTCATTTGCTTGGATGA
TGACATAGTAGCGAGTCTTATCCTCATAGTTGAGTCTTTTCCTCAGTACCACGTTGCCAGTCA
GCATGAGTGGAATTTCAAAGGTGTCGTTGGATGTCGGATCTTCTGGGTTGTACTGAATCACGT
ATTCTATCTGTCCATTAGGGCCATCGTCTATGTCTGTAGCTCCATTGTCTCCCGAGAACCCCG
TGAATATCGTGGTGCCAACTGGAGTGAGCTCATTCACGGTGGCATAGTAGCTTTCATGCTTGA
ATGTGGGGGAGTTGTCATTCCGATCTCGCACCACGATGCGTACTTCATGATAGATAACTGTGC
CAACCTTCTTGTTGACACACTGGACTTGCACCACAATGGAGTGTATGTTCATTGGTGGGTCTC
TATCCAGAACTCTTCCGGTACTGTTCAGGAAAAGCATCTGTTTAACGGGGTCCAGCAACACCC
AGTAGTCCACGTTGTCCTTTAAAGAGAGCTCTATGGTGGGGTCTGGTCCTCCGGCAGTCCCCT
TAATCAACATGTTATCCACCAGAATTGTACCGTTTCGACTCTCTTCATCAATGGCCACGATAG
TAGCTGGTGGTCCTCCCCTAGCTAGTTTGCAATCCTCGTATTGCCAGTCATCGTCATACTGGC
CCCAGCTGACTACCAAGAGAGAGGCAATGAGGATCCCATGGGGTAAACACTTCCAGACAGCAA
ACTGTAGGAACAT (SEQ ID NO: 67)

Mouse mini-PCDH15-CD2-1-V8:

AAGGGCTGTGTTGTAACCTTCGGAGTTTGCGCCTGGAGATTTCTTGGGCTCTTCATCCTTCCT
TCTGTCATATTCTGGCACCTGAAAGCCCCAGGGGCCTCCGGAGAGACTCTCACTGGTACTGCT
GCTGCTGCTCAGTTCTGACTCTGACTCCTCACTTTCCACGCCCCTCTCCATGGAGACTGATTC
TGCACTGCCCTCCTCTGGGACATCCTGAGCCTCCAGGTCTGTGGACTCATCCATGGGAGCTGC
TTCGCTTTCTTCTCCTTCCTCTGCCCGTTCTTCCTCCTCTAGTGGGGGCTCTTCTTCCTCTTC
CACCGGGGGCTCCTCTCTCTTACCTTTCACCTCCTGGATTTCCTCGACCACAGGCCTTCTTCT
AGCCAGCACGATGTTTTTTCTTGCTTTCTCTCCCTCTGACTCAGTGGACTCAGACTCCTCTGA
CTCCGGGGTAGAGCTCTCCTCCGCTTCCTCAGATGGGGTCTCCGACTCTGATTCTTCAGTTGT
CTCGGACTCGCTGAACTCGGACTCCGTTTCTGTGTATTCTGTGTAGTCGCTGGACTCCTCCTC
TGACTCCACGGTGCTTTCGGTAGCTTCCTCCTGGTCTAGAGTCAGTTGAAGATAGTCTTTGTC
TTCTTCATCAAGGCGCCTCCTCCACTCCTCGCCCTCAAGGTCAATGCCTCTTTTCTCAGCGAG
ACCTCTGACTTTCTTAAAAATCATCGGGAATATCCTGGCTCTCTTCCACGTTGGGTATGTGGG
CTCAGCCGCTGGTGGCTTCTCAACGGTGACTACCACCTCCTCCTCACTAGGCTCTCTAATTTC
AACTTTGGGTTTTTTAACTTTCTCTGGCTCTACCTCTTCTTCTTCATATTCCTCTTCAGCTTC
ACCAATGACTTCGCCGTATTCCTCCTGTCCAGCAGGTGGCAGCAGTCGACGGCGACTTCCATA
CTGGGGCATCTCATACTTATGCATTGCGCTCTCTCCCAGTTCTTCATAGAGATGTGCTCCTGG
TGGTGGTGGTGGCGGGGGCGGGGGCGGCGCAGGCGCAGCTGGTACAGGAGCTGCAGGCTTGGC
TGCAGGCATAGCAGACTGAATTCTTGCGGTCTTCGTGCACTCAGCCTGGCGTACTTTAAACTG
TCGGTAGCTTACTAAGACGACCAAGATGGCTGGGATGCAACAGAGGATGATGATGAAGGCCAA
GGCCAGCAAGGCCCCTTCTGTGTACCCCAAGCTTTCTCCTCGCTTCTTGATGCTCGTCACTGC

CTCAGGTGTCCGAATCTCCAGAATGCGCCCTCCTTCCCCGTAATACGGCTGGAAGTCTTTATT
GATATCGAGCAGTTTGCCGTCCAGGAACTTAAAAAGCTCATTTCTGTCGATGGCTCTGTTGGT
CTGCGGGTCGATGGCATAGACAGTCAGGTCGCACTTGCTATAGTCTTCTAGGGAGTAGGCGTC
TCCATGGCGACGGGCACCTATGGACTCCACCACAACCTTGGCACCAGGAATTTGCTCCTGAAC
GTAGCGATCCAAAATCTCTGTAAGGTCTTCTATCTTCTTTTCCACTAGTGTAGGGGGCACATT
GGAGACAATGACCTGCATATCCAGTTGATTGACCACGGAGACCAGTACGTCTGCTTTCCCGCT
CAACCCCTTCCCGTAGTCGTCAGTTGCAATCACTTGAAACTTGAAGTAGGATCTTCTCATATT
GTGGAAGAGCATGGCTGTCTTGATGAGACCTGTGTATGTTTCCACCACAAACCCCTCTTTGCC
CTCTTTAATCGGCGGTATGATGAGCCGGTAGGCCATGGCACTGTAATTACCCGTGTCCCTGTC
GGTGGCCTTCACTCTGAGCACAGATGCGAACATCCTTGCGTCTTCAGACACACCTCCAATGTA
GAATTTCTTCTGGAACACTGGGGGGTTATCATCAATGTCCAACACCTTGATGTACAGTGTCAG
AGTTGAATGTCGAGGGTGGACTGCTCCATCTGTTGCCACGACAACCAGTTCATAGTGGTCCCT
GGCTTCCCTGTTCAGCTTCACGGCTGTGTAAATGCTCCCGTTGGATGTGATGCGGAAGAGGTT
GTTGAAGTTCCCCAGGCTGTAGTGAACTTGGCCGTTTATCCCAGCATCTGGGTCTGTTGCCCG
GACTTGACCCACAAAGGCATTGGCTTCTTCCTCCACCACAGAGAGGTTCCTGGGCAGATAGGG
ATCGAACACGGGAGCGTTATCATTTGCATCCATCACTCGGATATTGACCACGACTGGCTCACT
TTCTTGCACGCCATCAAACGCTGTTATCAGAAAGGTGTAGGTTTGCTGTTCCTCCCTGTCCAC
AGGTTGAAGCAGGGTGAGGTAGCGGGTGATACCAGTGGGTGTCACAGTGAAGACCGAGGTGTA
GTCATTCAGGAAGAGGTGGAGCTCTGGATCTTTTGTGTCTTCTATGTCTTTGTCCAGAGCTAC
AATTCTCAGAGGAGTGGTTAAGTTTAGGCTCTCAGAAATGGTGGCTCCCACTGGGGCGGATTC
CAGGATGTATCCTTGATAGCTGGGCATTGTGAAGTATGGACTCTGATTGTTTTCGTCTAGTAT
TTCGATGTGCAGACTAGCAAAGGCAGGAAGTGGGTGGCCATTGTCCTGCTCAGCCTTAATAAC
CAAATCAAATTTTTGATGGAAGTCTCTGTTTACTGGCTCCAGGAGAGTGAGTTCTGCAGTCCT
GGGATGCATATGGAAGAAGCGGGGGTAATCCTCAGGGGTGCCGACAAGGATGGAGTAGAGGAT
GCCAGGTCGATCAGATGGTGGTTGGATGTTTCGGTCCTGATCAATGGCTTGGATAGGTGGTGT
CACCAAAATAGGGTTCAGTTCTTCCGGAGTCCTCAGTTCAGGAATGGCAGCTTGGTAGGTGAG
TGGACGACAGTCACGTGTGTTTGGCACAAGAACACAAGGCAGAAACATAGGTCCCAGGTCAT
CTCCATCTAGAACATCTACTGTGAGGGTGGTGGTGGTTGTTCGCCTCTCATTCAGATTTTGTG
CACGGTCATTTGCTTGGATGATGACATAGTAGCGAGTCTTATCCTCATAGTTGAGTCTTTTCC
TCAGTACCACGTTGCCAGTCAGCATGAGTGGAATTTCAAAGGTGTCGTTGGATGTCGGATCTT
CTGGGTTGTACTGAATCACGTATTCTATCTGTCCATTAGGGCCATCGTCTATGTCTGTAGCTC
CATTGTCTCCCGAGAACCCCGTGAATATCGTGGTGCCAACTGGAGTGAGCTCATTCACGGTGG
CATAGTAGCTTTCATGCTTGAATGTGGGGGAGTTGTCATTCCGATCTCGCACCACGATGCGTA
CTTCATGATAGATAACTGTGCCAACCTTCTTGTTGACACACTGGACTTGCACCACAATGGAGT
GTATGTTCATTGGTGGGTCTCTATCCAGAACTCTTCCGGTACTGTTCAGGAAAAGCATCTGTT
TAACGGGGTCCAGCAACACCCAGTAGTCCACGTTGTCCTTTAAAGAGAGCTCTATGGTGGGGT
CTGGTCCTCCGGCAGTCCCCTTAATCAACATGTTATCCACCAGAATTGTACCGTTTCGACTCT
CTTCATCAATGGCCACGATAGTAGCTGGTGGTCCTCCCCTAGCTAGTTTGCAATCCTCGTATT
GCCAGTCATCGTCATACTGGCCCCAGCTGACTACCAAGAGAGAGGCAATGAGGATCCCATGGG
GTAAACACTTCCAGACAGCAAACTGTAGGAACAT (SEQ ID NO: 68)

Mouse mini-PCDH15-CD2-1-V9:

ATGTTCCTACAGTTTGCTGTCTGGAAGTGTTTACCCCATGGGATCCTCATTGCCTCTCTCTTG
GTAGTCAGCTGGGGCCAGTATGACGATGACTGGCAATACGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACTATCGTGGCCATTGATGAAGAGAGTCGAAACGGTACAATTCTGGTGGAT
AACATGTTGATTAAGGGGACTGCCGGAGGACCAGACCCCACCATAGAGCTCTCTTTAAAGGAC

AACGTGGACTACTGGGTGTTGCTGGACCCCGTTAAACAGATGCTTTTCCTGAACAGTACCGGA
AGAGTTCTGGATAGAGACCCACCAATGAACATACACTCCATTGTGGTGCAAGTCCAGTGTGTC
AACAAGAAGGTTGGCACAGTTATCTATCATGAAGTACGCATCGTGGTGCGAGATCGGAATGAC
AACTCCCCCACATTCAAGCATGAAAGCTACTATGCCACCGTGAATGAGCTCACTCCAGTTGGC
ACCACGATATTCACGGGGTTCTCGGGAGACAATGGAGCTACAGACATAGACGATGGCCCTAAT
GGACAGATAGAATACGTGATTCAGTACAACCCAGAAGATCCGACATCCAACGACACCTTTGAA
ATTCCACTCATGCTGACTGGCAACGTGGTACTGAGGAAAAGACTCAACTATGAGGATAAGACT
CGCTACTATGTCATCATCCAAGCAAATGACCGTGCACAAAATCTGAATGAGAGGCGAACAACC
ACCACCACCCTCACAGTAGATGTTCTAGATGGAGATGACCTGGGACCTATGTTTCTGCCTTGT
GTTCTTGTGCCAAACACACGTGACTGTCGTCCACTCACCTACCAAGCTGCCATTCCTGAACTG
AGGACTCCGGAAGAACTGAACCCTATTTTGGTGACACCACCTATCCAAGCCATTGATCAGGAC
CGAAACATCCAACCACCATCTGATCGACCTGGCATCCTCTACTCCATCCTTGTCGGCACCCCT
GAGGATTACCCCCGCTTCTTCCATATGCATCCCAGGACTGCAGAACTCACTCTCCTGGAGCCA
GTAAACAGAGACTTCCATCAAAAATTTGATTTGGTTATTAAGGCTGAGCAGGACAATGGCCAC
CCACTTCCTGCCTTTGCTAGTCTGCACATCGAAATACTAGACGAAAACAATCAGCCCCCAGTG
TTCCAGAAGAAATTCTACATTGGAGGTGTGTCTGAAGACGCAAGGATGTTCGCATCTGTGCTC
AGAGTGAAGGCCACCGACAGGGACACGGGTAATTACAGTGCCATGGCCTACCGGCTCATCATA
CCGCCGATTAAAGAGGGCAAAGAGGGGTTTGTGGTGGAAACATACACAGGTCTCATCAAGACA
GCCATGCTCTTCCACAATATGAGAAGATCCTACTTCAAGTTTCAAGTGATTGCAACTGACGAC
TACGGGAAGGGGTTGAGCGGGAAAGCAGACGTACTGGTCTCCGTGGTCAATCAACTGGATATG
CAGGTCATTGTCTCCAATGTGCCCCCTACACTAGTGGAAAAGAAGATAGAAGACCTTACAGAG
ATTTTGGATCGCTACGTTCAGGAGCAAATTCCTGGTGCCAAGGTTGTGGTGGAGTCCATAGGT
GCCCGTCGCCATGGAGACGCCTACTCCCTAGAAGACTATAGCAAGTGCGACCTGACTGTCTAT
GCCATCGACCCGCAGACCAACAGAGCCATCGACAGAAATGAGCTTTTTAAGTTCCTGGACGGC
AAACTGCTCGATATCAATAAAGACTTCCAGCCGTATTACGGGGAAGGAGGGCGCATTCTGGAG
ATTCGGACACCTGAGGCAGTGACGAGCATCAAGAAGCGAGGAGAAAGCTTGGGGTACACAGAA
GGGGCCTTGCTGGCCTTGGCCTTCATCATCATCCTCTGTTGCATCCCAGCCATCTTGGTCGTC
TTAGTAAGCTACCGACAGTTTAAAGTACGCCAGGCTGAGTGCACGAAGACCGCAAGAATTCAG
TCTGCTATGCCTGCAGCCAAGCCTGCAGCTCCTGTACCAGCTGCGCCTGCGCCGCCCCCGCCC
CCGCCACCACCACCACCAGGAGCACATCTCTATGAAGAACTGGGAGAGAGCGCAATGCATAAG
TATGAGATGCCCCAGTATGGAAGTCGCCGTCGACTGCTGCCACCTGCTGGACAGGAGGAATAC
GGCGAAGTCATTGGTGAAGCTGAAGAGGAATATGAAGAAGAAGAGGTAGAGCCAGAGAAAGTT
AAAAAACCCAAAGTTGAAATTAGAGAGCCTAGTGAGGAGGAGGTGGTAGTCACCGTTGAGAAG
CCACCAGCGGCTGAGCCCACATACCCAACGTGGAAGAGAGCCAGGATATTCCCGATGATTTTT
AAGAAAGTCAGAGGTCTCGCTGAGAAAAGAGGCATTGACCTTGAGGGCGAGGAGTGGAGGAGG
CGCCTTGATGAAGAAGACAAAGACTATCTTCAACTGACTCTAGACCAGGAGGAAGCTACCGAA
AGCACCGTGGAGTCAGAGGAGGAGTCCAGCGACTACACAGAATACACAGAAACGGAGTCCGAG
TTCAGCGAGTCCGAGACAACTGAAGAATCAGAGTCGGAGACCCCATCTGAGGAAGCGGAGGAG
AGCTCTACCCCGGAGTCAGAGGAGTCTGAGTCCACTGAGTCAGAGGGAGAGAAAGCAAGAAAA
AACATCGTGCTGGCTAGAAGAAGGCCTGTGGTCGAGGAAATCCAGGAGGTGAAAGGTAAGAGA
GAGGAGCCCCCGGTGGAAGAGGAAGAAGAGCCCCCACTAGAGGAGGAAGAACGGGCAGAGGAA
GGAGAAGAAAGCGAAGCAGCTCCCATGGATGAGTCCACAGACCTGGAGGCTCAGGATGTCCCA
GAGGAGGGCAGTGCAGAATCAGTCTCCATGGAGAGGGGCGTGGAAAGTGAGGAGTCAGAGTCA
GAACTGAGCAGCAGCAGCAGTACCAGTGAGAGTCTCTCCGGAGGCCCCTGGGGCTTTCAGGTG
CCAGAATATGACAGAAGGAAGGATGAAGAGCCCAAGAAATCTCCAGGCGCAAACTCCGAAGGT
TACAACACAGCCCTT (SEQ ID NO: 152)

Mouse mini-PCDH15-CD2-1-V10:

ATGTTCCTACAGTTTGCTGTCTGGAAGTGTTTACCCCATGGGATCCTCATTGCCTCTCTCTTG
GTAGTCAGCTGGGGCCAGTATGACGATGACTGGCAATACGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACTATCGTGGCCATTGATGAAGAGAGTCGAAACGGTACAATTCTGGTGGAT
AACATGTTGATTAAGGGGACTGCCGGAGGACCAGACCCCACCATAGAGCTCTCTTTAAAGGAC
AACGTGGACTACTGGGTGTTGCTGGACCCCGTTAAACAGATGCTTTTCCTGAACAGTACCGGA
AGAGTTCTGGATAGAGACCCACCAATGAACATACACTCCATTGTGGTGCAAGTCCAGTGTGTC
AACAAGAAGGTTGGCACAGTTATCTATCATGAAGTACGCATCGTGGTGCGAGATCGGAATGAC
AACTCCCCCACATTCAAGCATGAAAGCTACTATGCCACCGTGAATGAGCTCACTCCAGTTGGC
ACCACGATATTCACGGGGTTCTCGGGAGACAATGGAGCTACAGACATAGACGATGGCCCTAAT
GGACAGATAGAATACGTGATTCAGTACAACCCAGAAGATCCGACATCCAACGACACCTTTGAA
ATTCCACTCATGCTGACTGGCAACGTGGTACTGAGGAAAAGACTCAACTATGAGGATAAGACT
CGCTACTATGTCATCATCCAAGCAAATGACCGTGCACAAAATCTGAATGAGAGGCGAACAACC
ACCACCACCCTCACAGTAGATGTTCTAGATGGAGATGACCTGCCCCCAGTGTTCCAGAAGAAA
TTCTACATTGGAGGTGTGTCTGAAGACGCAAGGATGTTCGCATCTGTGCTCAGAGTGAAGGCC
ACCGACAGGGACACGGGTAATTACAGTGCCATGGCCTACCGGCTCATCATACCGCCGATTAAA
GAGGGCAAAGAGGGGTTTGTGGTGGAAACATACACAGGTCTCATCAAGACAGCCATGCTCTTC
CACAATATGAGAAGATCCTACTTCAAGTTTCAAGTGATTGCAACTGACGACTACGGGAAGGGG
TTGAGCGGGAAAGCAGACGTACTGGTCTCCGTGGTCAATCAACTGGATATGCAGGTCATTGTC
TCCAATGTGCCCCCTACACTAGTGGAAAAGAAGATAGAAGACCTTACAGAGATTTTGGATCGC
TACGTTCAGGAGCAAATTCCTGGTGCCAAGGTTGTGGTGGAGTCCATAGGTGCCCGTCGCCAT
GGAGACGCCTACTCCCTAGAAGACTATAGCAAGTGCGACCTGACTGTCTATGCCATCGACCCG
CAGACCAACAGAGCCATCGACAGAAATGAGCTTTTTAAGTTCCTGGACGGCAAACTGCTCGAT
ATCAATAAAGACTTCCAGCCGTATTACGGGGAAGGAGGGCGCATTCTGGAGATTCGGACACCT
GAGGCAGTGACGAGCATCAAGAAGCGAGGAGAAAGCTTGGGGTACACAGAAGGGGCCTTGCTG
GCCTTGGCCTTCATCATCATCCTCTGTTGCATCCCAGCCATCTTGGTCGTCTTAGTAAGCTAC
CGACAGTTTAAAGTACGCCAGGCTGAGTGCACGAAGACCGCAAGAATTCAGTCTGCTATGCCT
GCAGCCAAGCCTGCAGCTCCTGTACCAGCTGCGCCTGCGCCGCCCCCGCCCCCGCCACCACCA
CCACCAGGAGCACATCTCTATGAAGAACTGGGAGAGAGCGCAATGCATAAGTATGAGATGCCC
CAGTATGGAAGTCGCCGTCGACTGCTGCCACCTGCTGGACAGGAGGAATACGGCGAAGTCATT
GGTGAAGCTGAAGAGGAATATGAAGAAGAAGAGGTAGAGCCAGAGAAAGTTAAAAAACCCAAA
GTTGAAATTAGAGAGCCTAGTGAGGAGGAGGTGGTAGTCACCGTTGAGAAGCCACCAGCGGCT
GAGCCCACATACCCAACGTGGAAGAGAGCCAGGATATTCCCGATGATTTTTAAGAAAGTCAGA
GGTCTCGCTGAGAAAAGAGGCATTGACCTTGAGGGCGAGGAGTGGAGGAGGCGCCTTGATGAA
GAAGACAAAGACTATCTTCAACTGACTCTAGACCAGGAGGAAGCTACCGAAAGCACCGTGGAG
TCAGAGGAGGAGTCCAGCGACTACACAGAATACACAGAAACGGAGTCCGAGTTCAGCGAGTCC
GAGACAACTGAAGAATCAGAGTCGGAGACCCCATCTGAGGAAGCGGAGGAGAGCTCTACCCCG
GAGTCAGAGGAGTCTGAGTCCACTGAGTCAGAGGGAGAGAAAGCAAGAAAAAACATCGTGCTG
GCTAGAAGAAGGCCTGTGGTCGAGGAAATCCAGGAGGTGAAAGGTAAGAGAGAGGAGCCCCCG
GTGGAAGAGGAAGAAGAGCCCCCACTAGAGGAGGAAGAACGGGCAGAGGAAGGAGAAGAAAGC
GAAGCAGCTCCCATGGATGAGTCCACAGACCTGGAGGCTCAGGATGTCCCAGAGGAGGGCAGT
GCAGAATCAGTCTCCATGGAGAGGGGCGTGGAAAGTGAGGAGTCAGAGTCAGAACTGAGCAGC
AGCAGCAGTACCAGTGAGAGTCTCTCCGGAGGCCCCTGGGGCTTTCAGGTGCCAGAATATGAC
AGAAGGAAGGATGAAGAGCCCAAGAAATCTCCAGGCGCAAACTCCGAAGGTTACAACACAGCC
CTT (SEQ ID NO: 153)

Full length mouse PCDH15 CD2 isoform coding sequence:

ATGTTCCTACAGTTTGCTGTCTGGAAGTGTTTACCCCATGGGATCCTCATTGCCTCTCTCTTG
GTAGTCAGCTGGGGCCAGTATGACGATGACTGGCAATACGAGGATTGCAAACTAGCTAGGGGA
GGACCACCAGCTACTATCGTGGCCATTGATGAAGAGAGTCGAAACGGTACAATTCTGGTGGAT
AACATGTTGATTAAGGGGACTGCCGGAGGACCAGACCCCACCATAGAGCTCTCTTTAAAGGAC
AACGTGGACTACTGGGTGTTGCTGGACCCCGTTAAACAGATGCTTTTCCTGAACAGTACCGGA
AGAGTTCTGGATAGAGACCCACCAATGAACATACACTCCATTGTGGTGCAAGTCCAGTGTGTC
AACAAGAAGGTTGGCACAGTTATCTATCATGAAGTACGCATCGTGGTGCGAGATCGGAATGAC
AACTCCCCCACATTCAAGCATGAAAGCTACTATGCCACCGTGAATGAGCTCACTCCAGTTGGC
ACCACGATATTCACGGGGTTCTCGGGAGACAATGGAGCTACAGACATAGACGATGGCCCTAAT
GGACAGATAGAATACGTGATTCAGTACAACCCAGAAGATCCGACATCCAACGACACCTTTGAA
ATTCCACTCATGCTGACTGGCAACGTGGTACTGAGGAAAAGACTCAACTATGAGGATAAGACT
CGCTACTATGTCATCATCCAAGCAAATGACCGTGCACAAAATCTGAATGAGAGGCGAACAACC
ACCACCACCCTCACAGTAGATGTTCTAGATGGAGATGACCTGGGACCTATGTTTCTGCCTTGT
GTTCTTGTGCCAAACACACGTGACTGTCGTCCACTCACCTACCAAGCTGCCATTCCTGAACTG
AGGACTCCGGAAGAACTGAACCCTATTTTGGTGACACCACCTATCCAAGCCATTGATCAGGAC
CGAAACATCCAACCACCATCTGATCGACCTGGCATCCTCTACTCCATCCTTGTCGGCACCCCT
GAGGATTACCCCCGCTTCTTCCATATGCATCCCAGGACTGCAGAACTCACTCTCCTGGAGCCA
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CCACTTCCTGCCTTTGCTAGTCTGCACATCGAAATACTAGACGAAAACAATCAGAGTCCATAC
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CCACCTGGTGGAGTTCCTACAAAAGATCCAGAGCTCCACCTCTTCCTGAATGACTACACCTCG
GTCTTCACTGTGACACCCACTGGTATCACCCGCTACCTCACCCTGCTTCAACCTGTGGACAGG
GAGGAACAGCAAACCTACACCTTTCTGATAACAGCGTTTGATGGCGTGCAAGAAAGTGAGCCA
GTCGTGGTCAATATCCGAGTGATGGATGCAAATGATAACACGCCCACCTTCCCTGAAATCTCC
TATGATGTCTATGTTTACACAGACATGAGTCCTGGGGACAGCGTCATTCAGCTGACAGCGGTA
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TTCGTGATCAACAAGACCACAGGGCTGGTGAGCATTGCACCAGGCGTGGAGCTGATCGTGGGA
CAGACGTATGCGCTCACAGTGCAGGCTTCGGACAACGCCCCGCCTGCAGAAAGAAGGCACTCC
ATCTGCACAGTGTACATCGAGGTGCTTCCTCCTAACAACCAGAGCCCTCCCCGCTTCCCGCAG
CTGATGTACAGTCTGGAAGTCAGCGAGGCCATGAGGATCGGTGCTATTTTATTAAATCTACAG
GCAACTGATCGAGAGGGAGATCCAATCACATATGCCATCGAGAATGGAGACCCTCAGAGAGTT
TTTAATCTTTCAGAAACCACAGGGATTCTCAGCCTAGGGAAGGCTCTAGACCGCGAGAGCACA
GACCGCTACATCCTCATCGTCACAGCCTCAGATGGCAGACCGGATGGAACCTCAACTGCCACT
GTGAACATAGTGGTGACGGACGTCAATGACAACGCTCCCGTGTTCGATCCCTATCTGCCCAGG
AACCTCTCTGTGGTGGAGGAAGAAGCCAATGCCTTTGTGGGTCAAGTCCGGGCAACAGACCCA
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ACATCCAACGGGAGCATTTACACAGCCGTGAAGCTGAACAGGGAAGCCAGGGACCACTATGAA
CTGGTTGTCGTGGCAACAGATGGAGCAGTCCACCCTCGACATTCAACTCTGACACTGTACATC
AAGGTGTTGGACATTGATGATAACAGTCCTGTTTTTACCAATTCAACGTACACAGTTGTCGTT
GAAGAGAATCTGCCAGCCGGGACCTCCTTTCTTCAAATAGAGGCCAAGGATGTTGACCTTGGA
GCCAATGTGTCATATCGGATCAGAAGCCCAGAAGTGAAACACCTTTTTGCACTGCATCCATTC
ACTGGAGAATTGTCTCTTCTGAGGAGTTTGGATTATGAGGCCTTTCCGGACCAGGAGGCAAGC
ATCACATTCTTGGTGGAGGCCTTTGACATTTATGGGACTATGCCACCTGGTATAGCAACAGTC
ACGGTAATTGTGAAGGACATGAATGACTACCCTCCAGTGTTTAGCAAACGCATCTACAAGGGG
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GCCAGTATTTTTGATGTAGAGGAAGATTCTGGAAGAGTAGTAACCCGCGTCAATCTTAATGAA
GAGCCTACTACGATTTTCAAGCTGGTGGTTGTGGCTTTTGATGACGGCGAACCTGTGATGTCC
AGCAGTGCCACGGTGAGAATTCTTGTCTTACATCCTGGAGAGATCCCACGCTTCACCCAAGAG
GAATACAGACCTCCTCCTGTAAGTGAGCTTGCGGCCAGAGGGACTGTAGTTGGTGTCATTTCT
GCTGCTGCCATTAATCAGAGCATCGTGTACTCCATTGTGGCAGGAAATGAGGAAGACAAGTTT
GGAATCAACAATGTCACTGGGGTCATCTATGTGAATTCACCATTGGATTACGAGACAAGGACC
AGCTATGTGCTCCGGGTACAAGCAGATTCTCTGGAAGTGGTCCTTGCCAATCTCCGAGTCCCT
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TTCCAGAAGAAATTCTACATTGGAGGTGTGTCTGAAGACGCAAGGATGTTCGCATCTGTGCTC
AGAGTGAAGGCCACCGACAGGGACACGGGTAATTACAGTGCCATGGCCTACCGGCTCATCATA
CCGCCGATTAAAGAGGGCAAAGAGGGGTTTGTGGTGGAAACATACACAGGTCTCATCAAGACA
GCCATGCTCTTCCACAATATGAGAAGATCCTACTTCAAGTTTCAAGTGATTGCAACTGACGAC
TACGGGAAGGGGTTGAGCGGGAAAGCAGACGTACTGGTCTCCGTGGTCAATCAACTGGATATG
CAGGTCATTGTCTCCAATGTGCCCCCTACACTAGTGGAAAAGAAGATAGAAGACCTTACAGAG
ATTTTGGATCGCTACGTTCAGGAGCAAATTCCTGGTGCCAAGGTTGTGGTGGAGTCCATAGGT
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GGGGCCTTGCTGGCCTTGGCCTTCATCATCATCCTCTGTTGCATCCCAGCCATCTTGGTCGTC
TTAGTAAGCTACCGACAGTTTAAAGTACGCCAGGCTGAGTGCACGAAGACCGCAAGAATTCAG
TCTGCTATGCCTGCAGCCAAGCCTGCAGCTCCTGTACCAGCTGCGCCTGCGCCGCCCCCGCCC
CCGCCACCACCACCACCAGGAGCACATCTCTATGAAGAACTGGGAGAGAGCGCAATGCATAAG
TATGAGATGCCCCAGTATGGAAGTCGCCGTCGACTGCTGCCACCTGCTGGACAGGAGGAATAC
GGCGAAGTCATTGGTGAAGCTGAAGAGGAATATGAAGAAGAAGAGGTAGAGCCAGAGAAAGTT
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CCACCAGCGGCTGAGCCCACATACCCAACGTGGAAGAGAGCCAGGATATTCCCGATGATTTTT
AAGAAAGTCAGAGGTCTCGCTGAGAAAAGAGGCATTGACCTTGAGGGCGAGGAGTGGAGGAGG
CGCCTTGATGAAGAAGACAAAGACTATCTTCAACTGACTCTAGACCAGGAGGAAGCTACCGAA
AGCACCGTGGAGTCAGAGGAGGAGTCCAGCGACTACACAGAATACACAGAAACGGAGTCCGAG
TTCAGCGAGTCCGAGACAACTGAAGAATCAGAGTCGGAGACCCCATCTGAGGAAGCGGAGGAG
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GAACTGAGCAGCAGCAGCAGTACCAGTGAGAGTCTCTCCGGAGGCCCCTGGGGCTTTCAGGTG
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TACAACACAGCCCTTTAG (SEQ ID NO: 69)

Full length mouse PCDH15 CD2 isoform amino acid sequence:

MFLQFAVWKCLPHGILIASLLVVSWGQYDDDWQYEDCKLARGGPPATIVAIDEESRNGTILVD
NMLIKGTAGGPDPTIELSLKDNVDYWVLLDPVKQMLFLNSTGRVLDRDPPMNIHSIVVQVQCV
NKKVGTVIYHEVRIVVRDRNDNSPTFKHESYYATVNELTPVGTTIFTGFSGDNGATDIDDGPN
GQIEYVIQYNPEDPTSNDTFEIPLMLTGNVVLRKRLNYEDKTRYYVIIQANDRAQNLNERRTT
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RNIQPPSDRPGILYSILVGTPEDYPRFFHMHPRTAELTLLEPVNRDFHQKFDLVIKAEQDNGH
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VVVNIRVMDANDNTPTFPEISYDVYVYTDMSPGDSVIQLTAVDADEGSNGEISYEILVGGKGD
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DRYILIVTASDGRPDGTSTATVNIVVTDVNDNAPVFDPYLPRNLSVVEEEANAFVGQVRATDP
DAGINGQVHYSLGNFNNLFRITSNGSIYTAVKLNREARDHYELVVVATDGAVHPRHSTLTLYI
KVLDIDDNSPVFTNSTYTVVVEENLPAGTSFLQIEAKDVDLGANVSYRIRSPEVKHLFALHPF
TGELSLLRSLDYEAFPDQEASITFLVEAFDIYGTMPPGIATVTVIVKDMNDYPPVFSKRIYKG
MVAPDAVKGTPITTVYAEDADPPGMPASRVRYRVDDVQFPYPASIFDVEEDSGRVVTRVNLNE
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RLDEEDKDYLQLTLDQEEATESTVESEEESSDYTEYTETESEFSESETTEESESETPSEEAEE
SSTPESEESESTESEGEKARKNIVLARRRPVVEEIQEVKGKREEPPVEEEEEPPLEEEERAEE
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PEYDRRKDEEPKKSPGANSEGYNTAL (SEQ ID NO: 70)

Mouse TM + CD1 cytoplasmic domain coding sequence:

GGGGCCTTGCTGGCCTTGGCCTTCATCATCATCCTCTGTTGCATCCCAGCCATCTTGGTCGTC
TTAGTAAGCTACCGACAGTTTAAAGTACGCCAGGCTGAGTGCACGAAGACCGCAAGAATTCAG
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CCACTGTCACTTCCTCCTCCTCCTCGGCCACCAGCTCCCCGCCTCTTCCCACAGCCTCCTTCC
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CACGCCAGAGAAACCACGTCTACGACACAGCCACCAGCATCCAACCCGCAGTGGGGGGCAGAA
CCCCACAGACATCCAAAAGGGATCCTCAGACATGTGAAAAACTTGGCAGAGCTCGAGAAATCA
GTGTCTAACATGTACAGTCACATAGAAAAAAACTGCCCACCTGCAGATCCCTCAAAACTACAC
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GTTAGAGTTGTTGAGGGAATTGACGTGCAACCTCACAGTCAATCAACATCTTTGTAA (SEQ ID NO: 154)

Mouse TM + CD2 cytoplasmic domain coding sequence:

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Mouse TM + CD3-1 cytoplasmic domain coding sequence (includes coding and non-coding regions):

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GGGTTTTTTTTCCTTTCAGCCAAGGTTTCTATGTTCTGGTAAGGAAGTTTGTTTTGATTATTG
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CAAAGCACAGGGGAAATATGTAGGTACTGTTAGTCTTAAAAAGAATTAACATAGATAGTATTT
ACATGGAAGTATATATAAGGAAATTTGTGCCTGGTTTTCCTAGAAGGGCATGAGAAGTTTCTT
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CTGAAAACCCTAAGAGCTGTCACAGAATTCCAACTGAATAGCATCCCAAAGGACCTTCTTAAA
GTACAGGAAACGGCTGTCCTGAGGTCCCCACTGTCAGCAATGATGTTAAAACATGTTTGCCCT
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CAGAAAGCAAGAAGTCATTGGATATTAATTCATGAAAGGAGCCATCGTCTTTCTTCCTTTCAC
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ATTACACAATGTTTTACAAATAAATTTCTTTTTGAAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO: 156)

Each construct was evaluated for proper membrane targeting and proper position of the extracellular domain outside of the cell, using live-cell labeling with an antibody to the PCDH15 N-terminal (EC1). An antibody was raised against amino acids 80–96 of PCDH15, within EC1.

Antibodies were previously validated using both fluorescence and electron microscopy immunolabeling in a *Pcdh15-null* mouse (FIG. 1G).

Eight mini-PCDH15-IRES-GFP constructs were tested in cells shown to have no native PCDH15 expression (HEK293 and CHO cells). Pcdh15-CD1-IRES-GFP and mini-Pcdh15-IRES-GFP constructs were successfully transfected in HEK cells. GFP signal were used to identify transfected cells, while the anti-Pcdh15 antibody labeling against a common region of Pcdh15 (EC1-EC2) showed a cell membrane labeling pattern. Non-transfected control (bottom right panels) showed no signal for anti-PCDH15 antibody binding, confirming the antibody specificity. The presence of untransfected HEK cells is confirmed using brightfield imaging. All but one have shown significant expression levels in CHO cells, with the V5 variant reporting the highest expression levels (FIG. 1H and FIG. 1I).

To determine whether AAV-delivered mini-PCDH15 is trafficked to the correct location and forms tip links, fluorescence confocal and immunogold scanning electron microscopy (SEM) were used, with our antibody to the N-terminus. If the PCDH15 N-terminus is properly extracellular, the N-terminal antibody would label live cells. If properly trafficked and functional in hair cells, mini-PCDH15 should be located at the tips of all but the tallest

stereocilia of a hair bundle and tip links should be observed in SEM. HEK cells were transfected with eight mini-PCDH15s and with wild-type PCDH15 (control) to express successful mini candidates and test whether the PCDH15 N-terminus is properly extracellular. Fluorescence confocal and immunogold electron microscopy were used, with an antibody to the N-terminus to determine location of the protein. All these mini-PCDH15s were properly targeted to the plasma membrane (FIG. 1M).

Further, HEK cells were transfected with either Pcdh15-CD1, Pcdh15-CD2, or mini-Pcdh15 variants then labeled with 12 nm gold particles (bright dots on the images) using anti-Pcdh15 antibody. Scanning electron microphotographs report high surface labeling density in cells transfected with native Pcdh15 and all mini-Pcdh15 variants, with in-frame untransfected control cells free of labels. This result suggests efficient transport of Pcdh15 variants to the cell membrane, and indicates proper positioning of the EC domains extracellularly similar to native Pcdh15 in hair cells (FIG. 1J).

Full length Pcdh15-CD1 and mini-PCDH15 variants were then individually expressed in HEK-NC cell line lacking N-Cadherin (*Yamagata et al., 2018*), mixed with an equal number of HEK-NC cells expressing CDH23, and incubated on a rotating shaker at 100 rpm for 12 hours. PCDH15 expressing cells also expressed GFP, while CHD23 transfected cells were co-transfected with mCherry. Aggregates were observed using bright field microscopy to access their size (left panels), followed by fluorescence microscopy to evaluate the cell composition of the aggregates. In all cases, the aggregates report heteromeric interaction between PCDH15 and CHD23, but not controls, expressing only GFP and mCherry (bottom right panel), suggesting mini-Pcdh15 variants successfully bind Cdh23 and are likely to form tip links when expressed in hair cells (FIG. 1K).

Kinetics of PCDH15-CDH23 binding with biolayer interferometry, and zero-force off rates that match those calculated from single-molecule force spectroscopy were measured. Biolayer interferometry can quantify protein-protein interaction kinetics under 'zero force' conditions. A "bait" protein (CDH23) is immobilized on the surface of the optical sensor, and the sensor is then incubated with "prey" binding partners (cell lysate with mini-PCDH15 variants). Protein-protein interaction is read out as an optical interference signal. On- and off-rates will be analyzed to calculate binding affinity. Because the PCDH15-CDH23 interaction is Ca2+ sensitive, whether mini-PCDH15 constructs have the same Ca2+ sensitivity will be

assessed. As an additional control would be PCDH15-R113G, a deafness mutant with impaired binding to CDH23.

Single-molecule force spectroscopy is used to test the strength of binding between mini-PCDH15 variants and CDH23. PCDH15 is immobilized on PEG-passivated glass beads using a covalent SNAP linkage, and CDH23 is similarly attached to beads. Using laser tweezers, a pair of beads are brought together, allow a bond to form, and then separate the beads until the cadherins unbind, measuring unbinding force (FIG. 1L). In this way, whether the mini-PCDH15-CDH23 bond can withstand similar forces as that of wt PCDH15-CDH23 is tested. To measure the unfolding strength of individual mini-PCDH15 proteins, N- and C-termini of mini-PCDH15 extracellular domains to are attached different glass beads, and pull to measure the unfolding force. Successful mini-PCDH15s will unfold at forces equal to or near the full-length PCDH15 extracellular domain.

To test whether the miniPcdh15-Cdh23 interaction can withstand a force applied by a myosin motor, the nano-SPD technique was used (Bird JE, Barzik M, Drummond MC, et al. Harnessing molecular motors for nanoscale pulldown in live cells. *Mol Biol Cell.* 2017;28(3):463–475. doi:10.1091/mbc.E16-08-0583). It has been shown that native EGFP-tagged CDH23, when pulled by myosin-X, can transport mCherry-tagged PCDH15 to the tips of fillopodia. As additional controls, these results were further validated using mutant forms of PCDH15 (PCDH15-R113G and PCDH15-I108N) that are known to weaken the PCDH15-CDH23 interaction. The miniPCDH15s were tested for their interaction with CDH23 to withstand force applied by myosin motor. In FIG. 4, Nano-SPD assay for PCDH15 binding to CDH23 under force are shown. Top left shows schematic of myosin motor and linked cadherins: myosin-X with a GFP-nanotrap binds to GFP, pulling CDH-23-GFP (bait) to the tips of filopodia. If the prey protein (PCDH-15-mCherry) interacts with the bait, both will be trafficked to the tips of filopodia. Positive controls are shown in the top panels. In the middle panel, the images show experimental groups and the results demonstrate that mini-PCDH15 version 7 was properly drawn to the tips by CDH23. The bottom panel show negative control groups, and the results indicate wild-type PCDH15 with an inactivating deafness mutation (I108N) is not drawn to the tips by CDH23. Images from left to right are: GFP-tagged CDH23 was drawn to the tips of filopodia by the myosin; mCherry-tagged control PCDH15 was drawn to the tips by CDH23; and a merged image shows co-localization.

To investigate the ability of mini-PCDH15s to rescue hair-cell function, a *Pcdh15fl/fl* mouse line was created by inserting loxP sites flanking *Pcdh15* exon 31 which encodes the single transmembrane domain. The mice are crossed to a *Gfi1-Cre* line to delete exon 31 in hair cells. *Gfi1-Cre* expression in cochlear hair cells begins at E15.5 (Yang et al, 2010), likely allowing brief expression of wild-type *Pcdh15* in hair cells. A *Myo15-Cre* mouse (Caberlotto et al., 2011) allowing longer expression of wild-type *Pcdh15* before deletion was used. The best mini-PCDH15s are expressed in inner ear hair cells of PCDH15-KO (*Pcdh15fl/fl*× *Gfi1-Cre*) mice. Each mini-PCDH15 coding sequence, driven by a short promoter, are delivered with an AAV9-PHP.B vector. Vectors are injected into inner ears of PCDH15-KO mice at P0; cochlear explants will be cultured at P4 and kept for 1-5 more days before testing.

To test physiological function, FM1-43 dye loading and single-cell electrophysiology is used to assess mechanotransduction in PCDH15-null hair cells. AAV9-PHP.B encoding mini-PCDH15s are injected into inner ears of PCDH15-KO mice at P0. Cochleas are removed at P4, and cultured for 1-3 days before being tested. no dye loading in *non-injected* PCDH15-KO mice should be observed, after the Cre eliminates endogenous *Pcdh15* expression and tip links are lost. *After injection*, if mini-PCDH15 is functional, dye loading of most hair cells should be observed. For single-cell electrophysiology, receptor currents from individual cells with a patch pipet while stimulating individual hair bundles are recorded with a glass probe. If mini-PCDH15 is functional, the receptor currents will be within the normal receptor currents of 500-800 pA.

To test functional hearing, mini-PCDH15s are expressed using AAV9-PHP.B and are injected at P0. Mice are allowed to survive to adulthood (4 weeks) and hearing with the auditory brainstem evoked response (ABR) will be tested. In normal mice, mid-frequency sounds as quiet at 30 dB evoke an ABR; in KO mice, sounds of 100 dB do not. If mini-PCDH15 constructs are functional, substantial rescue of hearing is expected, with ABRs evoked at 40-50 dB. Auditory function will be retested at 8 weeks to assess long-term rescue. Distortion product otoacoustic emissions (DPOAEs) is measured to specifically assess the functional rescue of outer hair cells, since AAVs are less efficient in transducing outer hair cells.

As in human Usher syndrome, mice lacking functional PCDH15 also have vestibular dysfunction. Virus injected into mouse cochlea diffuses to the vestibular organs and should

rescue balance (György et al., 2017). To test PCDH15-KO mice, circling behavior is observed, quantified by video recording, and swimming. Normal mice swim with their heads above the surface; mutant mice have no sense of 'up' and tumble underwater. Similarly to the rescue of a different deaf mouse model (György et al., 2017), mini-PCDH15 injected mice show no circling and should swim normally.

Pcdh15fl/fl×Gfi1-Cre mice show disrupted bundle morphology, lack anti-PCDH15 antibody labelling on stereocilia (FIG. 1G), are profoundly deaf, and have a vestibular deficit evidenced by circling behavior. However the bundle morphology deficit in *Pcdh15fl/fl× Gfi1-Cre* mice is much less pronounced than in *Av3j* mice (Alagramam et al., 2011), and hair cells can be loaded with FM1-43 for a few days postnatally, indicating delayed deletion of *Pcdh15*. AAV injection into neonatal cochlea is routine in the Corey laboratory, and AAV9-PHP.B transduces 50-70% of OHCs and often more.

To translate the mouse studies to human model of Usher 1F, fibroblasts from a human Usher 1F patient carrying the R245X mutation are obtained. These will be further differentiated into 3D inner ear organoids.

Whether *mouse* mini-PCDH15s can rescue the bundle morphology and the mechanotransduction function in *human* hair cells are tested using an inner ear organoid system. Bundle morphology is tested with SEM, and mechanotransduction following mini-PCDH15 expression using FM1-43 dye uptake and single-cell physiology. Functional mini-PCDH15 expression should improve bundle morphology, and rescue dye uptake and transduction currents by forming functional tip links. Immunogold SEM will assess localization of exogenous PCDH15 at the tips of stereocilia in organoid hair cells.

Fluorescence confocal and scanning electron microscopy were used to evaluate hair-cell bundle morphology during bundle development. Stereocilia bundle orientation in cochlear whole mounts were evaluated; actin was stained with phalloidin to visualize stereocilia bundles. In the *Pcdh15fl/fl,Gfi1-Cre+* mouse, these showed disrupted bundle morphology in hair cells at P5. Finally, the morphology of inner and outer hair-cell stereocilia bundles were evaluated using scanning electron microscopy (SEM) in P1, P6, and P8 mice. Severe bundle disorganization was detected even at the earliest age evaluated (FIG. 1N). FIG. 1N shows SEM photomicrographs of *Pcdh15fl/fl,Gfi1-Cre+* (left) and *Pcdh15fl/fl,Gfi1-Cre-* (right) OHCs stereocilia bundles at P1 (upper panels) and P5 (lower panels). Hair-cell

mechanotransduction was visually assessed by a brief application of FM1-43, known to enter hair cells through functional mechanotransduction channels. FM1-43 loading at P5 by *Pcdh15fl/fl,Gfi1-Cre+* hair cells was decreased compared to hair cells in mice without Cre-mediated deletion. The presence of PCDH15 was assessed with immunofluorescent and immunogold anti-Pcdh15 antibody labeling, and confirmed that PCDH15 is completely absent in *Pcdh15fl/fl,Gfi1-Cre+* mice at P5.

Next, hearing in *Pcdh15fl/fl,Gfi1-Cre+* mice were evaluated. Auditory Brainstem Response (ABR) and Distortion Product Otoacoustic Emission (DPOAE) thresholds in response to pure tone stimuli were measured in these mice. As expected, *Pcdh15fl/fl,Gfi1-Cre+* mice were profoundly deaf at P21. All versions of mini-PCDH15 are injected to the mice to evaluate recue of hearing loss in these mice.

Further, another mouse model, *Pcdh15fl/fl,Myo15-Cre+* mice, were developed to model late onset PCDH15 deficit. Because the *Pcdh15fl/fl,Gfi1-Cre+* mouse has severe bundle pathology at the time of the attempt rescue by viral injection (P1), it was of concern that the observed functional deficit was an indirect effect of the bundle disorganization. Therefore, *Pcdh15fl/fl,Myo15-Cre+* mice was created with a late-onset PCDH15 deficit. This mouse is homozygous for a floxed exon that encodes the critical transmembrane domain of PCDH15. It is heterozygous for Myo15-Cre, which drives expression of Cre recombinase under the Myo15 promoter, a late-onset, hair-cell-specific promoter. Stereocilia bundle morphology in cochleas was evaluated in which actin was stained with phalloidin and also used SEM. The data showed normal bundle morphology and presence of tip links in hair cells at P6 (FIG. 1O). FIG. 1O shows SEM photomicrographs of *Pcdh15fl/fl,Gfi1-Cre-* (upper panel) and Pcdh15fl/fl,Gfi1-Cre+(lower pannel) stereocilia bundles at P6. Finally, it was confirmed that *Pcdh15fl/fl, Gfi1-Cre+* mice were profoundly deaf at P35 and P60. Thus the pathology observed at P35 and P60 was a consequence of disrupting the mechanotransduction process and not just the bundle disorganization.

In order to test the viral transduction efficiency in delivering transgene to cochlear hair cells, ssAAV9-PHP.B-CMV584bp-eGFP-noWPRE-BGHpolyA virus were used to infect cochlear hair cells in C57BL/6 mice. Because the hybrid CBA promoter, previously tested in cochlea, is too large to fit into a single AAV vector (~5 kb capacity) even with the shortest mini-PCDH15s (V4, V7, V8), a short CMV promoters was used in the mouse cochlea. An

AAV plasmid which has a CMV584 bp promoter with eGFP reporter, no WPRE and BGH polyA was used as a backbone for packaging V4, V7, and V8 mini-PCDH15s. The CMV584bp-eGFP-noWPRE-BGHpolyA vector was packaged in the AAV9-PHP.B capsid and its efficiency in the cochlea was tested. Robust eGFP expression in both IHCs and OHCs thought the cochlea in C57BL/6 mice at P5 were observed (**FIG. 3A**).

In addition, three versions of mouse miniPCDH15 AAV vector were constructed and tested for their abilities in preventing hearing loss.

An exemplary nucleic acid sequence for AAV2-CMV584bp-V4-mouse miniPCDH15-noWPRE-BGHpolyA is set forth in SEQ ID NO: 116:

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An exemplary nucleic acid sequence for AAV2-CMV584bp-V7-mouse miniPCDH15-noWPRE-BGHpolyA is set forth in SEQ ID NO: 117:

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CGTCGGGCGACCTTTGGTCGCCCGGCCTCAGTGAGCGAGCGAGCGCGCAGAGAGGGAGTGGCC
A (SEQ ID NO: 117)

An exemplary nucleic acid sequence for AAV2-CMV584bp-V8-mouse miniPCDH15-noWPRE-BGHpolyA is set forth in SEQ ID NO: 118:

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TCAGTCTCCATGGAGAGGGGCGTGGAAAGTGAGGAGTCAGAGTCAGAACTGAGCAGCAGCAGC
AGTACCAGTGAGAGTCTCTCCGGAGGCCCCTGGGGCTTTCAGGTGCCAGAATATGACAGAAGG
AAGGATGAAGAGCCCAAGAAATCTCCAGGCGCAAACTCCGAAGGTTACAACACAGCCCTTTAG
CTCGAGTCTAGAGTCGACTAGAGCTCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCC
ATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCT
TTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGG
TGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGAGAG
ATCTAGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAG
GCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGTCGCCCGGCCTCAGTGAGCGAGCGA
GCGCGCAGAGAGGGAGTGGCCA (SEQ ID NO: 118)

Pcdh15fl/fl,Myo15-Cre+ mice were used to test rescue of hearing with miniPCDH15 versions. Auditory brainstem evoked response (ABR), an electrical signal recorded from the back of the head which is generated by the neurons carrying auditory information to the brain was tested; ABR is a standard measure of cochlear function. Mice lacking the Myo15-Cre and therefore expressing normal PCDH15 respond to sounds of intensity as low as 30 dB. The sensitivity expressed as the lowest intensity that can elicit an ABR signal is plotted against the frequency of the stimulus; normal mice can hear sounds as quiet as 30 dB in middle frequencies from 8 to 16 kHz. Mice with the Myo15-Cre and therefore deleting PCDH15 have little or no response, usually not responding to the loudest tested sound of 85 dB at any frequency.

Three miniPCDH15 constructs as described above were tested. rAAV having AAV9-PHP.B capsid encapsulating AAV genome encoding the miniPCDH15 was injected into the cochleas of new born mice (postnatal day 1) that had the Myo15-Cre and would normally lack hearing. Three weeks later, hearing was tested with ABR. miniPCDH15-version 8 (V8)

showed no rescue of hearing: at most frequencies there was no response at 85 dB, the same as the untreated deaf mutant (FIG. 3B). A second miniPCDH15, version 4 (V4), showed good rescue, with thresholds in the middle frequencies of ~55 dB, the level of a normal conversation (FIG. 3C). The third miniPCDH15, version 7 (V7), showed the best rescue, lowering thresholds to below 50 dB, only about 20 dB less sensitive than normal hearing. In human, 20-40 dB loss of sensitivity is considered mild hearing loss (FIG. 3D and FIG. 3E).Non-human primate can also be modeled for efficacy of AAV9.PHP.B-mini-PCDH15. Previous data shows AV9-PHP.B encoding GFP shows very strong label throughout the organ of Corti, and in most other cells of the cochlear duct. In a wild-type NHP, localization and toxicity can be tested. Using the best mini-PCDH15s constructs from mouse and organoid experiments, primate mini-PCDH15s are designed. An epitope tag is inserted at an exposed non-conserved loop of the extracellular MAD12 domain (P1285, N1323 or G1353) , or the N-terminus. The tag can be either 3xHA, SNAP-tag or the high affinity tandem GCN tag (Zhao et al., 2016). Function of the tagged protein is validated in mouse cochlea as in Aim 1b. An AAV9-PHP.B with the mini-PCDH15 coding sequence is constructed, and is injected through the round window membrane in *Macaca fascicularis* monkeys (György et al., 2018). After one month, animals are sacrificed and expression of tagged mini-PCDH15 assessed with an antibody to the tag. Robust expression in hair cells, and label near the tips of the shorter stereocilia should be observed. Toxicity is assessed by testing auditory sensitivity with ABR before viral injection and again before sacrifice. Sections of inner ear is also assessed for inflammation and cell death. RNA Scope technique with mini-PCDH15-specific probes is also used to detect mRNA in the inner ear tissue.

MATERIALS AND METHODS

Animals: mice were matched for experimental animals to littermate controls. Mice are back-crossed to a common background for at least 8 generations. Mouse strains that lack the Cdh23 Ahl mutation that causes age-related hearing loss, and test new mice, regardless of background, for that mutation were used. Experimental groups are age- and gender-matched.

Histological: Specificity of antibodies is documented in the Authentication of Key Biological Resources. For counting labeled cells, standard protocols for thresholding positive cells were used.

Physiological: To ensure reproducibility for ABR recordings, standard protocols for placement of acoustic systems and ABR electrodes were derived. For measurement of receptor current, the peak current observed in the first three minutes were detected with a standard, automated stimulus protocol.

Behavioral: Video analysis of movement for assessing vestibular function is computer-analyzed. Assessment of swimming ability is scored by an observer but in a strict, second-by-second scoring of mouse position. In both cases, the behavioral tester to experimental group are blinded.

Biolayer Interferometry

A C-terminal SNAP-tag and His tag onto the extracellular domain of PCDH15 is cloned, then immobilize purified SNAP-tagged PCDH15 onto a streptavidin-functionalized probe in an Octet Red 384 by reacting the SNAP-tag with a benzylguanine-biotin ligand. Then, His-tagged CDH23 extracellular domain, constructed as a parallel dimer by fusion with human Fc domains, are affinity purified and analyzed by SDS-PAGE, and the protein identity confirmed by mass spectroscopy. PCDH15 and CDH23 on- and off-rates are analyzed to assess the binding affinity. For each, Ca2+ sensitivity are tested.

Force Spectroscopy

An N-terminal SpyTag into the C-terminal SNAP-tagged PCDH15 construct was cloned for biolayer interferometry. A double stranded DNA handle is created by PCR using a forward primer with a 5' benzylguanine and a reverse primer with a 3' dual biotin. Protein will be reacted with the DNA handle via a SNAP-tag to benzylguanine reaction and purified by His-tag purification. The protein-DNA hybrid is immobilized onto streptavidin-functionalized microspheres. Another DNA handle containing a 5' cysteine-labeled SpyCatcher protein immobilized via a thiol-maleimide reaction and a 3' dual biotin is be coated onto separate streptavidin microspheres. Each microsphere is held in a dual-beam optical tweezer, a single and continuous DNA tether formed by a SpyTag-SpyCatcher reaction, and the tether pulled apart to stretch the PCDH15 molecule. Using high speed video tracking, the unfolding force of WT- and mini-PCDH15 molecules is measured under a constant force loading rate. Unfolding force is tested in 30 μM and 2 mM [Ca2+].

EM of inner ear organoid systems.

Organoids are cut out with small amounts of surrounding matrigel, fixed with 2.5% glutaraldehyde and further processed using our SEM sample preparation routine (Indzhykulian et al., 2013; Vogl et al, 2016). After critical point drying, the organoids are mounted on an SEM holder and gently cracked open with a needle to expose the inner lumen and expose the bundles. For TEM and FIB-SEM, the organoids are embedded in a resin using our TEM sample preparation routine (Scheffer et al., 2015).

Mouse RWM Injection in Neonatal Mice

P0–P1 CD1 and C57BL/6 pups were anesthetized by hypothermia and then kept on an ice pack during the procedure. As previously described, a small incision was made underneath the external ear. The incision was enlarged, and soft tissues were pushed apart using an eyelid retractor to expose the bulla. Then the round window niche was localized visually. Covering connective tissue was removed to expose the round window.

Adult Mouse Injection

4-week-old mice were anesthetized with ketamine (100 mg/kg) and xylazine (20 mg/kg) through an intraperitoneal injection. Both eyes were protected by an application of eye gel (GenTeal lubricant eye gel). The fur behind the left ear was shaved with a sterile razor, and the surgical area was cleansed two times with antiseptic solution, isolated with sterile drapes, and swabbed along the proposed incision with 10% povidone-iodine. a surgical procedure similar to that described by Suzuki *et al.*18 A small (10- to 15-mm) postauricular skin incision was made. After exposing the facial nerve and the sternocleidomastoid muscle by blunt dissection, the tissue covering the temporal was separated and retracted using the magnetic retractor set. A small hole was made with a microprobe in the exposed bony wall of the posterior canal. After 2–3 min for leakage of perilymph to stop, the tip of a MicroFil 35G needle was inserted into the hole. The aperture between the MicroFil needle and the hole was sealed with tissue fragments and cyanoacrylate glue (3 M Vetbond Tissue Adhesive) and visually assessed for lack of fluid leakage. 1 mL viral suspension at 155 nL/min was injected using the Nanoliter 2000 Injector (World Precision Instruments). After the injection was completed, the plastic needle remained in the canal for 5 min and then was cut off proximally to the canal. The hole was filled in with tissue and sealed with glue. The wound was closed with 5-0 Vicryl-coated sutures and swabbed with 10% povidone-iodine. The mouse was placed on a heating pad until full recovery. Animals received an intraperitoneal injection of

meloxicam (0.01 mL/g body weight) after surgery and once more within the first 24 hr. Injected mice were checked daily for 5 days following surgery.

Mouse ABR

The ABR assay was performed using a Tucker Davis Technologies System III workstation. Mice were anesthetized by intraperitoneal injection of a ketamine (100 mg/kg)/xylazine (10 mg/kg) cocktail. Anesthetized mice were then placed on a heating pad, and electrodes were placed subcutaneously in the vertex, underneath the left or right ear, and on the back near the tail. Tone stimuli of 4, 5.6, 8, 11.2, 16, 22, 32, and 45.3 kHz were calibrated with a precision microphone system (PS9200 Kit; ACO Pacific), using the TDT SigCal software package. The recorded signals were band-pass filtered (300 Hz to 3 kHz) and amplified 100,000 times. The number of acquisition trials was set to 500 averages. Maximum stimulus intensity was set to 95 dB peak SPL with attenuation decreasing from 85 dB to 0 dB SPL at 5-dB intervals. Band-pass filters (500–3,000 Hz) were applied to the traces before analysis.

Mouse Retina

Animals were handled in accordance with the statement of the "Animals in Research Committee" of the Association for Research in Vision and Ophthalmology (Rockville, MD, USA), and protocols were approved by the local institutional committee (Service vétérinaire du canton de Vaud, Lausanne, Switzerland). Adult C57BL/6 mice were anesthetized with a reversible anesthetic regimen composed of ketamine and medetomidine (ketamine, 30–60 mg/kg, Parker Davis; medetomidine, 0.5–1 mg/kg, Graeub), and the anesthesia was reversed with the injection of atipamezole (0.5–1 mg/kg, Graeub). For subretinal injections, a transcleral approach was used, and the procedure was visualized in the posterior chamber with a microscope and a coverslip covering the cornea surrounded with Viscotears (Novartis, Basel, Switzerland). AAV9-PHP.B-CBA-GFP vector (1 mL) was injected into the sub-retinal space of adult mice through a Hamilton syringe with a 34G needle (BGB Analytik).

Scanning Electron Microscopy

Organ of Corti explants were dissected at P1 and P5 in L-15 medium and fixed with 2.5% glutaraldehyde in 0.1 M cacodylate buffer (pH 7.2) supplemented with 2 mM CaCl2 for 1–2 hr at room temperature. For older (P30) animals, after intracardial perfusion with 4% paraformaldehyde and 1% glutaraldehyde, temporal bones were decalcificated overnight in

10% EDTA (pH 7.2–7.4) for 3–4 days at 4C. After unpeeling cochlear bone and removing the stria vascularis and tectorial membrane, the cochlear coils were isolated; divided into apical, middle, and basal turns; and postfixed with 2.5% glutaraldehyde in 0.1 M cacodylate buffer (pH 7.2) supplemented with 2 mM CaCl2 for 1–2 hr at room temperature. They were rinsed three times in 0.1 M cacodylate buffer (pH 7.2), washed in distilled water, dehydrated in an ascending series of ethanol concentrations, and criticalpoint dried from liquid CO2. Samples were then mounted on aluminum stubs with carbon conductive tabs and sputter-coated with 5 nm platinum, and then imaged in a field-emission scanning electron microscope (Hitachi S-4700).

NHP Cochlea

NHP studies were performed at Charles River Laboratories (Montreal, ON, Canada) according to animal use guidelines and approved procedures. The first cynomolgus monkey (Macaca fascicularis) (animal #1002) was a male, age 2.6 years, weighing 4 kg. The second animal (animal #3501) was a female, age 3.1 years, weighing 3.2 kg. The animals were anesthetized by intramuscular injection of a cocktail (ketamine, 10 mg/kg; xylazine, 0.6 mg/kg; and glycopyrrolate,0.01 mg/kg) following overnight food deprivation, intubated, andmaintained with oxygen and isoflurane during surgery. During the procedure, the following were administered to improve recovery: warmed lactated Ringer's solution intravenously (10 ml/kg/hr), cefazolin (20 mg/kg every 20–90 min), and topical antibiotics to the surgical site. The RWM was exposed using a trans-mastoid approach. Beginning with a low microscopic magnification, the temporal muscles were retracted exposing the supramastoid crest and the external cartilaginous portion of the ear canal. En route to the middle ear and with increasing magnification, mastoid air cells were burred very closely to the cartilaginous portion of the ear canal, and the bony portion thinned until the fossa incudis was reached, exposing the incus. A 1- to 2-mm facial recess was then performed with awareness of the horizontal semicircular canal, the facial nerve, and the tympanic membrane. The chorda tympani was retracted and/or resected, since it was not possible to preserve it without damaging the critical surrounding structures while allowing necessary exposure of the round window niche. In this species, the RWM is 0.6 mm in diameter.

Statistics

All experiments are designed to identify the most appropriate statistical analysis methods, to plan randomization and blinding, and to calculate sample sizes that provide high statistical reliability while minimizing the number of animals. Additional design tools, such as The Experimental Design Assistant from NC3Rs, are used to plan the experiment and analysis workflow for statistical reliability. To minimize bias, observers during analysis of any outcome measure that is not computer driven are blinded, *e.g.* ABR thresholds and cell counts. Mice and non-human primates of both sexes, are randomly selected. The sex of Usher 1F patients contributing fibroblasts are random. Prism software was used. p values < 0.05 were considered statistically significant.

Example 2: Engineering of mini-PCDH15 linker sequence between EC domains

In a full-length PCDH15 protein, the last five amino acids of an EC domain immediately preceding the next EC domain is the linking region between the two EC domains (linkers). Depending on the amino acid sequences of these linkers, they can be flexible or rigid. Some linkers may have different calcium ion binding capacities (e.g., from 0 to 3 Ca^{2+}). The presence, absence, or quantity of the Ca^{2+} may be important for proper function of the PCDH15. Linkers between the EC domains of PCDH15 have been previously described (e.g., Sotomayor et al, A partial calcium-free linker confers flexibility to inner-ear protocadherin-15, *Structure.* 2017 Mar 7; 25(3): 482–495.) Due to the deletion of certain EC domains in mini-PCDH15, some EC domains are connected artificially, and the succeeding EC domain is connected to the preceding one with a linker different from a full-length PCDH15. For example, in mini-PCDH15 V1, EC3 is connected with EC5, and the linker sequence is the last five amino acids of EC3 (DENNQ), as opposed to the situation in a full-length PCDH15, where EC5 is connected to EC4 with the last five amino acids of EC4 (DANDN).

When connecting two EC domains that are not connected in a full-length PCDH15 (e.g., EC3 connected to EC5 in mini-PCDH15 V1 and V5, EC4 connected to EC8 in mini-PCDH15 V2, EC3 connected to EC8 in mini-PCDH15 V3, EC7 connected to EC11 in mini-PCDH15 V5 and V8, EC4 connected to EC7 in mini-PCDH15 V6 and V8, EC8 connected to EC11 in mini-PCDH15 V6 and V7, EC3 connected to EC9 in mini-PCDH15 V4, EC3 connected to EC7 in mini-PCDH15 V7, EC3 connected to EC11 in mini-PCDH15 V9, and

EC2 connected to EC11 in mini-PCDH15 V10), the linking region may or may not affect the function of the miniPCDH15. One skilled in the art would understand that any of the EC domains of PCDH15 may be artificially connected to another EC domain in engineering of the mini-PCDH15. Non-limiting examples of linkers between the EC domains artificially connected in the mini-PCDH15 are shown in the Table 2.

The effect of the linkers between EC domains on the function of the mini-PCDH15 were investigated by structural modeling. mini-PCDH15 Version 4, 7, and 8 - the same versions tested in mice for their abilities to rescue hearing in Example 1 (FIGs. 3B-3E) were modeled. Interestingly, both V4 (FIG. 5A) and V7 (FIG. 5B) modeled well, and were predicted to retain the overall structural architecture of the full length PCDH15.

In contrast, the structural modeling for V8 suggested that the artificial connections within the mini-PCDH15-V8, which did not show rescue in the mouse ear, are positioning the EC domains at angles that would likely affect the 2-point protein dimerization (FIG, 5C). The structural modeling suggested that in order to have two dimerization points along the mini-PCDH15-v8 molecule, the EC11-MAD12 domains must be positioned away from the EC7. And the the chain linking EC7 and EC11 is disrupted, suggesting that that linker is not sufficient to span the gap to enable a proper positioning (FIG. 5C). The modeling results suggested that the possibility of V8 to form a functional dimeric structure is low, which is consistent with the data obtained from ABR testing showing that mini-PCDH15 V8 at its current state is unable to rescue hearing. However, the linkers between the artificially connected EC domains can be engineered to confer desired flexibility or Ca binding capacity. Some of the amino acid residues of the linkers can be replaced by amino acids S, A, G, or N, or amino acids S, A, G, or N can be added to the linker sequence to alter flexibility. A chimeric linker may be formed (e.g., to link EC3 and EC5, a chimeric linker between EC3 linker and EC4 linker can be engineered). Any of the mini-PCDH15 described herein may have altered linker sequence replacing the current linker sequences connecting the EC domains. Non-limiting examples of chimeric linkers between the artificially connected domains are shown in Table 3. It is known in the art that the second amino acid is not conserved and may not be crucial to linker function, therefore the second amino acid residual of the linker are shown as X, which can be any amino acid (e.g., R, G, E, A, P, V, I, M, P, E, V, or Q). Further, any of the known linkers can be used in connecting the EC domains of a miniPCDH15. Non-limiting

examples of known linkers include: GGGSGGG (SEQ ID NO: 139), GGSGG (SEQ ID NO: 140), DGNDN (SEQ ID NO: 141), DGNNN (SEQ ID NO: 142), DANDN (SEQ ID NO: 122), DANNN(SEQ ID NO: 143), GGNDN(SEQ ID NO: 144), GGNNN(SEQ ID NO: 145), GGSNN(SEQ ID NO: 146), GGSAA(SEQ ID NO: 147), AANDN(SEQ ID NO: 148), AANNN(SEQ ID NO: 149).

Example 3: Correction of c.773C>T mutation in genomic DNA with base editor.

Approximately 1% of Ashkenazi Jewish individuals carry a single C•G-to-T•A mutation in exon 8 of *PCDH15* (Brownstein et al., 2004). This alters the coding sequence to replace residue R245 with a stop codon (Ben-Yosef et al., 2003). About 1 in 40,000 offspring are homozygous, and the R245X mutation truncates the *PCDH15* protein, eliminating function and producing Usher 1F. Fortunately, the single base pair mutation which causes the R245X mutation makes it a suitable candidate for gene editing by ABEmax (Koblan et al., 2018).

To optimize gRNA sequences, base editor is first tested on the c.733C>T (p.R245X) mutation in vitro. Using lentivirus, a stable HEK293T cell line carrying 2 kb of the human PCDH15 cDNA, bearing the R245X mutation and encoding N-terminal FLAG and C-terminal MYC epitopes was generated by lentiviral transduction. These cells are transfected with the adenosine base editor (ABEmax, ABE7.1 and ABE 8e) along with the designed gRNAs to target the mutated base pair (FIG. 2A). Sequences of vectors encoding the gRNA are shown below in Table 5:

SEQ ID NO:	Vector	Sequence
173	JL42_gRNA 1_ALT	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGGTGGTGGTTCACCTCTCATTGTTTTAGAG CTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGA AAAAGTGGCACCGAGTCGGTGCTTTTTTTAAGCTTGGGCCGCTCG AGGTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAAAAG GCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGG CTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCC

		CCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTT ACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTT TCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTA AGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATT AGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGG TGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGC GCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCT TGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTT TGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGAT CCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAAC TCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTC ACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAA AGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATC AGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATA GTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGC TTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGC TCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGG GCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAG TCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTT AATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTG TCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAA CGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCG GTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCC GCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTT ACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGC TCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGA ACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAA CTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCC ACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGC GTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAG GGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTT TTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGC GGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTT CCGCGCACATTTCCCCGAAAAGTGCCACCT
174	JL42_gRNA 1+1	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGGTTCACCTCTCATTCAGATTTGTTTTAGA GCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTG AAAAAGTGGCACCGAGTCGGTGCTTTTTTTAAGCTTGGGCCGCTC

		GAGGTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAAAA GGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAG GCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCA GAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCC CCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCT TACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCT TTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGT TCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGA CCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGT AAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGAT TAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTG GTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTG CGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTC TTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGT TTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGA TCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAA CTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTT CACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTA AAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAAT CAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCAT AGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGG CTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACG CTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAG GGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCA GTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGT TAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGT GTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCA ACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGC GGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGC CGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCT TACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTA CTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTG CTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAG AACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAA ACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACC CACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAG CGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAA GGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCT TTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAG CGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGT TCCGCGCACATTTCCCCGAAAAGTGCCACCT
175	JL42_gRNA 1+2	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC

		GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGGGTTCACCTCTCATTCAGATTTGTTTTAG AGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTT GAAAAAGTGGCACCGAGTCGGTGCTTTTTTTAAGCTTGGGCCGCT CGAGGTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAAA AGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATA GGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTC AGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTC CCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGC TTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGC TTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCG TTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCG ACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGG TAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGA TTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGT GGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCT GCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCT CTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTG TTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAG ATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAA ACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCT TCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCT AAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAA TCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCA TAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGG GCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCAC GCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAA GGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCC AGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAG TTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGG TGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCC AACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAG CGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGG CCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTC TTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGT ACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTT GCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCA GAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAA AACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAAC CCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCA GCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAA AGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCC TTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGA GCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGG TTCCGCGCACATTTCCCCGAAAAGTGCCACCT
176	JL42_gRNA 1+3	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA

		TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGTGGTTCACCTCTCATTCAGATTTGTTTTA GAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACT TGAAAAAGTGGCACCGAGTCGGTGCTTTTTTTAAGCTTGGGCCGC TCGAGGTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAA AAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCAT AGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGT CAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTT CCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCG CTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCG CTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC GTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCC GACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCG GTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGG ATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAG TGGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATC TGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGC TCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTT GTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAA GATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAA AACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATC TTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATC TAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTA ATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCC ATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAG GGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCA CGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGA AGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATC CAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCA GTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTG GTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCC CAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAA GCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTG GCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCT CTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAG TACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGT TGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGC AGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGA AAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAA CCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACC AGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAA AAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTC CTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATG

		AGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGG GTTCCGCGCACATTTCCCCGAAAAGTGCCACCT
177	JL42_gRNA 1-1	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGTCACCTCTCATTCAGATTTGTTTTAGAGC TAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAA AAAGTGGCACCGAGTCGGTGCTTTTTTTAAGCTTGGGCCGCTCGA GGTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAAAAGG CCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGC TCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGA GGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCC CTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTA CCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTT CTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTC GCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACC GCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAA GACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTA GCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGT GGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCG CTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTT GATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTT GCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATC CTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACT CACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCA CCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAA GTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCA GTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAG TTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCT TACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCT CACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGG CCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGT CTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTA ATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGT CACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAAC GATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGG TTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCG CAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTA CTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACT CAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCT CTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAA CTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAAC TCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCA

		CTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCG TTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGG GAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTT TTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCG GATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTC CGCGCACATTTCCCCGAAAAGTGCCACCT
178	JL42_gRNA 1-2	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGCACCTCTCATTCAGATTTGTTTTAGAGCT AGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAAA AAGTGGCACCGAGTCGGTGCTTTTTTTAAGCTTGGGCCGCTCGAG GTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAAAAGGC CAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCT CCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAG GTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCC TGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTAC CGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTC TCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCG CTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCG CTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAG ACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAG CAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTG GCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGC TCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTG ATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTG CAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCC TTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTC ACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCAC CTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAG TATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAG TGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGT TGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTT ACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGC CGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTC TATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAA TAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTC ACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACG ATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGT TAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGC AGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTAC TGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTC

		AACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTC TTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAAC TTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACT CTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCAC TCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGT TTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGG AATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTT TCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGG ATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCC GCGCACATTTCCCCGAAAAGTGCCACCT
179	JL42_pFYF_gRNA_ABE_site_5	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGGATGAGATAATGATGAGTCAGTTTTAGAG CTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGA AAAAGTGGCACCGAGTCGGTGCTTTTTTTAAGCTTGGGCCGCTCG AGGTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAAAAG GCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGG CTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCC CCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTT ACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTT TCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTA AGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATT AGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGG TGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGC GCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCT TGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTT TGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGAT CCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAAC TCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTC ACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAA AGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATC AGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATA GTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGC TTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGC TCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGG GCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAG TCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTT AATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTG TCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAA

		CGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCG GTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCC GCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTT ACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGC TCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGA ACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAA CTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCC ACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGC GTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAG GGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTT TTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGC GGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTT CCGCGCACATTTCCCCGAAAAGTGCCACCT
180	JL42_pFYF _gRNA_AB E_site_13	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGGAAGATAGAGAATAGACTGCGTTTTAGAG CTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGA AAAAGTGGCACCGAGTCGGTGCTTTTTTTAAGCTTGGGCCGCTCG AGGTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAAAAG GCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGG CTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCC CCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTT ACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTT TCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTA AGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATT AGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGG TGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGC GCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCT TGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTT TGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGAT CCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAAC TCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTC ACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAA AGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATC AGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATA GTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGC TTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGC TCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGG

		GCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAG TCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTT AATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTG TCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAA CGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCG GTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCC GCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTT ACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGC TCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGA ACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAA CTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCC ACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGC GTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAG GGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTT TTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGC GGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTT CCGCGCACATTTCCCCGAAAAGTGCCACCT
181	JL42_pFYF _gRNA_AB E_site_16	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGGGGAATAAATCATAGAATCCGTTTTAGAG CTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGA AAAAGTGGCACCGAGTCGGTGCTTTTTTTAAGCTTGGGCCGCTCG AGGTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAAAAG GCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGG CTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCC CCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTT ACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTT TCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTA AGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATT AGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGG TGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGC GCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCT TGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTT TGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGAT CCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAAC TCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTC ACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAA AGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATC

		AGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATA GTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGC TTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGC TCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGG GCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAG TCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTT AATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTG TCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAA CGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCG GTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCC GCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTT ACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGC TCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGA ACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAA CTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCC ACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGC GTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAG GGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTT TTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGC GGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTT CCGCGCACATTTCCCCGAAAAGTGCCACCT
182	JL42_pFYF _gRNA1	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGTTCACCTCTCATTCAGATTTgttttagag ctagaaatagcaagttaaaataaggctagtccgttatcaacttga aaaagtggcaccgagtcggtgcTTTTTTTAAGCTTGGGCCGCTCG AGGTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAAAAG GCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGG CTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCC CCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTT ACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTT TCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTA AGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATT AGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGG TGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGC GCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCT TGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTT TGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGAT

		CCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAAC TCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTC ACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAA AGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATC AGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATA GTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGC TTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGC TCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGG GCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAG TCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTT AATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTG TCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAA CGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCG GTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCC GCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTT ACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGC TCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGA ACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAA CTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCC ACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGC GTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAG GGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTT TTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGC GGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTT CCGCGCACATTTCCCCGAAAAGTGCCACCT
183	JL42_pFYF _gRNA2	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGTCACCTCTCATTCAGATTTTGTTTTAGAG CTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGA AAAAGTGGCACCGAGTCGGTGCTTTTTTTAAGCTTGGGCCGCTCG AGGTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAAAAG GCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGG CTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCC CCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTT ACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTT TCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTA AGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATT AGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGG

		TGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGC GCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCT TGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTT TGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGAT CCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAAC TCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTC ACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAA AGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATC AGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATA GTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGC TTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGC TCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGG GCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAG TCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTT AATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTG TCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAA CGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCG GTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCC GCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTT ACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGC TCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGA ACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAA CTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCC ACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGC GTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAG GGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTT TTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGC GGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTT CCGCGCACATTTCCCCGAAAAGTGCCACCT
184	JL42_pFYF _gRNA3	GACGTCGCTAGCTGTACAAAAAAGCAGGCTTTAAAGGAACCAATT CAGTCGACTGGATCCGGTACCAAGGTCGGGCAGGAAGAGGGCCTA TTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTT AGAGAGATAATTAGAATTAATTTGACTGTAAACACAAAGATATTA GTACAAAATACGTGACGTAGAAAGTAATAATTTCTTGGGTAGTTT GCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACC GTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGG AAAGGACGAAACACCGTGGTGGTTCACCTCTCATTCGTTTTAGAG CTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGA AAAAGTGGCACCGAGTCGGTGCTTTTTTTAAGCTTGGGCCGCTCG AGGTACCTCTCTACATATGACATGTGAGCAAAAGGCCAGCAAAAG GCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGG CTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCC CCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTT ACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTT TCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTT

		CGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTA AGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATT AGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGG TGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGC GCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCT TGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTT TGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGAT CCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAAC TCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTC ACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAA AGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATC AGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATA GTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGC TTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGC TCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGG GCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAG TCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTT AATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTG TCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAA CGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCG GTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCC GCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTT ACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGC TCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGA ACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAA CTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCC ACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGC GTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAG GGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTT TTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGC GGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTT CCGCGCACATTTCCCCGAAAAGTGCCACCT

Amplification of R245X site was performed using PCR primer specific to lentivirus sequence. PCR products were sequenced using MiSeq Illumina platform. Several days post transfection, transfected cells can be harvested and assayed for base editing. Correction of DNA is assessed with high throughput sequencing (HTS) of PCR products synthesized with cDNA-specific primers, and base editing efficiency is determined by the Python utility *pysamstats*. Elimination of the stop and normal translation of the exogenous cDNA is assessed with western blot for the FLAG and cMYC tags (FIG. 2B).

The in vitro assay with fibroblasts from an Usher 1F patient carrying homozygous R245X mutations are repeated. Base editors and gRNAs are transiently transfected into induced pluripotent stem cells (iPSC) derived from cells taken from an Usher1F patient harboring the PCDH15$^{R245X/R245X}$ locus. Transfection of iPSCs is inefficient (~10% cells transfected). Genomic DNA was harvested and the R245X locus amplified by PCR, sequenced via MiSeq Illumina platform, and quantified using Python utility *pysamstats*. Again, successful base editing of genomic DNA is assayed with HTS of PCR products using primers within exon 8 (Ben-Yosef et al., 2003). Optimal gRNAs are confirmed on these human Usher 1F cells in vitro (FIG. 2C).

To determine editing efficiencies with guide varieties base editors ABEmax and ABE8e were transfected with gRNAs (vector sequences shown in Table 5, below) into HEK293T cells harboring the PCDH15 R245X mutation as in FIG. 2B. Results are shown in FIG. 2D. (#) refer to the variants of guide 1, displayed in Table 4. No significant differences are observed between the gRNA1 variants and gRNA1 except for (-2) and gRNA 1.

Base editing at R245X site using split-intein base editors was performed. HEK293T cells harboring the R245X mutation were transfected with plasmids containing gRNA1 and split-intein versions of ABEmax and ABE8e. Split-intein plasmids consist of: the ABE fused to the N-terminal Cas9 followed by an Nterminal Npu Intein sequence; and the C-term Npu intein sequence followed by the C-terminal Cas9 and U6promoter gRNA. QED Split-intein tests co-transfected two plasmids simultaneously, the C-terminal plasmid used for both N-term ABEmax and N-term ABE8e split-intein plasmid. Editing between ABE8e and ABE8e split-intein are not significantly different, whereas both are significantly better at editing than ABEmax (FIG. 2E).

Editing of genomic loci with intein editors was performed. FIG. 2F shows editing efficiencies of ABE7.1, max, and 8e at several previously validated genomic sites [Site 5 (GRCh38.p12 c20. 32752960 - 32752979); Site 13 (GRCh38.p13 c20.20116785 – 20116804); Site 16 (GRCh38.p12 c01.179826686 – 179826705)].. HEK293T cells were transfected with gRNAs to genomic targets and base editors in equal concentrations. Genomic DNA was harvested and subjected to PCR and Miseq Illumina sequencing.

Any effort to bring PCDH15 R245X gene therapy to the clinic will first require demonstration of rescue in a suitable mouse model. But base editors and gRNAs headed to the

clinic should recognize the *human* mutant DNA. A "humanized" mouse model in which 60 bp of the mouse exon 9 replaced with the equivalent sequence from human exon 8, with the R245X mutation was generated. Mouse exon 9 is present in almost all mouse PCDH15 splice forms (Ahmed et al., 2006), suggesting that a stop codon here truncates all mouse PCDH15 splice forms and cause deafness. Cyagen is producing the mouse for delivery in April 2019. Hair cell pathology and deafness in the homozygous humanized R245X mouse is assessed for lack of PCDH15, bundle morphology, FM1-43 dye loading, single-cell physiology, and ABR.

To test the efficacy of ABEmax on mutant mouse DNA *in vitro*, a fibroblast cell line harboring the R245X mutation is created from humanized mouse. ABEmax is delivered to these cells by transfection in culture and test the efficacy of base editing.

For gene therapy, ABEmax and gRNAs have to be delivered to affected cells in a viral vector. AAV vectors (AAV9-PHP.B or better variants developed by Core C) are used for efficient targeting to OHCs, but ABEmax coding sequence does not fit in AAV.

OTHER EMBODIMENTS

All of the features disclosed in this specification may be combined in any combination. Each feature disclosed in this specification may be replaced by an alternative feature serving the same, equivalent, or similar purpose. Thus, unless expressly stated otherwise, each feature disclosed is only an example of a generic series of equivalent or similar features.

From the above description, one skilled in the art can easily ascertain the essential characteristics of the present invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions. Thus, other embodiments are also within the claims.

EQUIVALENTS

While several inventive embodiments have been described and illustrated herein, those of ordinary skill in the art will readily envision a variety of other means and/or structures for performing the function and/or obtaining the results and/or one or more of the advantages described herein, and each of such variations and/or modifications is deemed to be within the

scope of the inventive embodiments described herein. More generally, those skilled in the art will readily appreciate that all parameters, dimensions, materials, and configurations described herein are meant to be exemplary and that the actual parameters, dimensions, materials, and/or configurations will depend upon the specific application or applications for which the inventive teachings is/are used. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific inventive embodiments described herein. It is, therefore, to be understood that the foregoing embodiments are presented by way of example only and that, within the scope of the appended claims and equivalents thereto, inventive embodiments may be practiced otherwise than as specifically described and claimed. Inventive embodiments of the present disclosure are directed to each individual feature, system, article, material, kit, and/or method described herein. In addition, any combination of two or more such features, systems, articles, materials, kits, and/or methods, if such features, systems, articles, materials, kits, and/or methods are not mutually inconsistent, is included within the inventive scope of the present disclosure.

All definitions, as defined and used herein, should be understood to control over dictionary definitions, definitions in documents incorporated by reference, and/or ordinary meanings of the defined terms.

All references, patents and patent applications disclosed herein are incorporated by reference with respect to the subject matter for which each is cited, which in some cases may encompass the entirety of the document.

The indefinite articles "a" and "an," as used herein in the specification and in the claims, unless clearly indicated to the contrary, should be understood to mean "at least one."

The phrase "and/or," as used herein in the specification and in the claims, should be understood to mean "either or both" of the elements so conjoined, i.e., elements that are conjunctively present in some cases and disjunctively present in other cases. Multiple elements listed with "and/or" should be construed in the same fashion, i.e., "one or more" of the elements so conjoined. Other elements may optionally be present other than the elements specifically identified by the "and/or" clause, whether related or unrelated to those elements specifically identified. Thus, as a non-limiting example, a reference to "A and/or B", when used in conjunction with open-ended language such as "comprising" can refer, in one embodiment, to A only (optionally including elements other than B); in another embodiment,

to B only (optionally including elements other than A); in yet another embodiment, to both A and B (optionally including other elements); etc.

As used herein in the specification and in the claims, "or" should be understood to have the same meaning as "and/or" as defined above. For example, when separating items in a list, "or" or "and/or" shall be interpreted as being inclusive, i.e., the inclusion of at least one, but also including more than one, of a number or list of elements, and, optionally, additional unlisted items. Only terms clearly indicated to the contrary, such as "only one of" or "exactly one of," or, when used in the claims, "consisting of," will refer to the inclusion of exactly one element of a number or list of elements. In general, the term "or" as used herein shall only be interpreted as indicating exclusive alternatives (i.e. "one or the other but not both") when preceded by terms of exclusivity, such as "either," "one of," "only one of," or "exactly one of." "Consisting essentially of," when used in the claims, shall have its ordinary meaning as used in the field of patent law.

As used herein in the specification and in the claims, the phrase "at least one," in reference to a list of one or more elements, should be understood to mean at least one element selected from any one or more of the elements in the list of elements, but not necessarily including at least one of each and every element specifically listed within the list of elements and not excluding any combinations of elements in the list of elements. This definition also allows that elements may optionally be present other than the elements specifically identified within the list of elements to which the phrase "at least one" refers, whether related or unrelated to those elements specifically identified. Thus, as a non-limiting example, "at least one of A and B" (or, equivalently, "at least one of A or B," or, equivalently "at least one of A and/or B") can refer, in one embodiment, to at least one, optionally including more than one, A, with no B present (and optionally including elements other than B); in another embodiment, to at least one, optionally including more than one, B, with no A present (and optionally including elements other than A); in yet another embodiment, to at least one, optionally including more than one, A, and at least one, optionally including more than one, B (and optionally including other elements); etc.

It should also be understood that, unless clearly indicated to the contrary, in any methods claimed herein that include more than one step or act, the order of the steps or acts of

the method is not necessarily limited to the order in which the steps or acts of the method are recited.

CLAIMS

What is claimed is:

1. An isolated nucleic acid comprising a transgene flanked by adeno-associated virus (AAV) inverted terminal repeats (ITRs), wherein the transgene encodes a mini-Protocadherin related 15 (mini-PCDH15).

2. The isolated nucleic acid of claim 1, wherein the mini-PCDH15 comprises a truncated extracellular portion of a full length PCDH15, wherein the full length PCDH15 comprises an extracellular domain as set forth in amino acid sequence of SEQ ID NO: 1.

3. The isolated nucleic acid of claims 1 or 2, wherein the mini-PCDH15 does not comprise one or more EC domains of the full-length PCDH15.

4. The isolated nucleic acid of any one of claims 1-3, wherein the mini-PCDH15 does not comprise amino acids residues 719 to 820 of SEQ ID NO: 1.

5. The isolated nucleic acid of any one of claims 1-4, wherein the mini-PCDH15 does not comprise amino acid residues 397 to 510 of SEQ ID NO: 1.

6. The isolated nucleic acid of any one of claims 1-5, wherein the mini-PCDH15 does not comprise amino acid residues 821 to 927 of SEQ ID NO: 1.

7. The isolated nucleic acid of any one of claims 1-6, wherein the mini-PCDH15 does not comprise amino acid residues 511 to 616 of SEQ ID NO: 1.

8. The isolated nucleic acid of any one of claims 1-7, wherein the mini-PCDH15 does not comprises amino acid residues 617 to 718 of SEQ ID NO: 1.

9. The isolated nucleic acid of any one of claims 1-8, wherein the mini-PCDH15 does not comprise amino acid residues 928 to 1036 of SEQ ID NO: 1.

10. The isolated nucleic acid of any one of claims 1-9, wherein the mini-PCDH15 does not comprise amino acid residues 1037 to1145 of SEQ ID NO: 1.

11. The isolated nucleic acid of any one of claims 1-10, wherein mini-PCDH15 does not comprise amino acid residues 266-396 of SEQ ID NO: 1.

12. The isolated nucleic acid of claim 11, wherein the mini-PCDH15 further comprises a transmembrane domain and a cytoplasmic domain, and optionally wherein the cytoplasmic domain of PCDH15 is a splice isoform.

13. The isolated nucleic acid of claim 12, wherein the splice isoform of PCDH15 is CD1, CD2, or CD3 splice isoform.

14. The isolated nucleic acid of any one of claims 1-13, wherein the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 31, 75 or 76.

15. The isolated nucleic acid of claim 14, wherein the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 32, 77 or 78.

16. The isolated nucleic acid of any one of claims 1-13, wherein the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 33, 79 or 80.

17. The isolated nucleic acid of claim 16, wherein the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 34, 81 or 82.

18. The isolated nucleic acid of any one of claims 1-13, wherein the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 35, 83 or 84.

19. The isolated nucleic acid of claims 18, wherein the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 36, 85 or 86.

20. The isolated nucleic acid of any one of claims 1-13, wherein the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 37, 87 or 88.

21. The isolated nucleic acid of claim 20, wherein the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 38, 89 or 90.

22. The isolated nucleic acid of any one of claims 1-13, wherein the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 39, 91 or 92.

23. The isolated nucleic acid of claim 22, wherein the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 40, 93 or 94.

24. The isolated nucleic acid of any one of claims 1-13, wherein the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 41, 95 or 96.

25. The isolated nucleic acid of claim 24, wherein the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 42, 97 or 98.

26. The isolated nucleic acid of any one of claims 1-13, wherein the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 43, 99 or 100.

27. The isolated nucleic acid of claim 26, wherein the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 44, 101 or 102.

28. The isolated nucleic acid of any one of claims 1-13, wherein the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 45, 103 or 104.

29. The isolated nucleic acid of claim 28, wherein the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 46, 105, or 106.

30. The isolated nucleic acid of any one of claims 1-13, wherein the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 71, 107, or 108.

31. The isolated nucleic acid of claim 30, wherein the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 72, 109, or 110.

32. The isolated nucleic acid of any one of claims 1-13, wherein the mini-PCDH15 comprises an amino acid sequence at least 80% identical to amino acid sequence of SEQ ID NO: 73, 111 or 112.

33. The isolated nucleic acid of claim 32, wherein the transgene encoding the mini-PCDH15 comprises a nucleic acid sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 74, 113, or 114.

34. The isolated nucleic acid of any one of claims 1-33, further comprises a promoter operably linked to the transgene encoding the mini-PCDH15.

35. The isolated nucleic acid of claim 31, wherein the promoter is a cytomegalovirus (CMV) promoter, a hybrid cytomegalovirus (CMV) immediate-early/chicken beta-actin promoter or chicken beta-actin promoter (CAG), a native promoter, or a minimal promoter.

36. The isolated nucleic acid of claim 35, wherein the native promoter is a Methyl-CpG Binding Protein 2 (MeCP2) promoter, a Ubiquitin-C (UbiC) promoter, a Bestrophin 1 (Best1) (retina native) promoter, a human red opsin (RedO) promoter, a human rhodopsin kinase (RK) promoter, a mouse cone arrestin (CAR) promotor, a human rhodopsin (Rho) promoter, a UV opsin-specific 1 (opn1sw1) promoter, a UV opsin-specific 2 (opn1sw2) promoter, an Opsin 1, Medium Wave Sensitive 2 (opn1mw2) promoter, an opsin 1, long-wave-sensitive 1 (opn1lw1) promoter, a blue cone specific promoter (sws2), an L-opsin (opn1lw1-cxxc1) promoter, a thyroid hormone receptor β (thrb) promoter, an LIM Homeobox 1a (lhx1a) promoter, a connexin 55.5 (cx55.5) promoter, a metabotropic glutamate receptor 6b (grm6b), a glial fibrillar acidic protein (gfap) promoter, a cone transducin alpha subunit (gnat2)promoter, a connexin 52.7 (cx52.7) promoter, a connexin 52.9 (cx52.9) promoter, a heat shock cognate 70-kd protein,-like (hsp70l) promoter, a yeast transcription activator protein- (GAL4-VP16) promoter, a upstream activation sequence (UAS), a visual system homeobox 1 (vsx1) promoter, or a rhodopsin (zop) promoter.

37. The isolated nucleic acid of claim 35, wherein the minimal promoter is minimal CMV, a CMV584bp promoter or a Jet T promoter.

38. The isolated nucleic acid of any one of claims 1-37, wherein the first region and/or the third region is an AAV2 ITR.

39. A vector, comprising the isolated nucleic acid of any one of claims 1-38.

40. The vector of claim 39, wherein the vector is a plasmid.

41. A host cell comprising the isolated nucleic acid of any one of claims 1-38, or the vector of claims 39 or 40.

42. A recombinant adeno-associated virus (rAAV) comprising:
(i) a capsid protein; and
(ii) the isolated nucleic acid of any one of claims 1 to 38.

43. The rAAV of claim 42, wherein the capsid protein is AAV5, AAV7, AAV8 or AAV9 capsid protein or a variant thereof.

44. The rAAV of claim 43, wherein the AAV capsid protein is AAV2.7m8 or AAV8BP2.

44. The rAAV of claim 43, wherein the AAV9 capsid variant is AAV9.PHP.B

45. The rAAV of claim 44, wherein the capsid protein comprises an amino acid sequence at least 90% identical to amino acid sequence of SEQ ID NO: 47.

46. The rAAV of claim 43, wherein the capsid protein is exoAAV.

47. The rAAV of claim 46, wherein the exoAAV is exoAAV1 or exoAAV9.

48. The rAAV of claim 43, wherein the capsid protein is Anc80.

49. The rAAV of any one of claims 42-48, wherein the rAAV is a single-stranded AAV (ssAAV) or a self-complementary AAV (scAAV).

50. The rAAV of any one of claims 42-48, wherein the rAAV is capable of delivering the transgene to a mammal.

51. The rAAV of claim 50, wherein the mammal is a human.

52. The rAAV of claim 50, wherein the mammal is a non-human mammal.

53. The rAAV of claim 52, wherein the non-human mammal is mouse, rat, or non-human primate.

54. The rAAV of any one of claims 42-53, wherein the rAAV is formulated for delivery to the cochlea or the retina.

55. The rAAV of any one of claims 54, wherein the rAAV is formulated for delivery to an outer hair cell (OHC), an inner hair cell (IHC), spiral ganglion neurons, stria vascularis, inner sulcus, spiral ligament, vestibular system.

56. The rAAV of any one of claims 54, wherein the rAAV is formulated for delivery to photoreceptor cells, and other cells in the retina within the photoreceptor inner and outer segments (IS), outer plexiform layer (OPL), inner nuclei layer (INL), ganglion cell layer (GCL), inner plexiform layer (IPL), and retinal pigment epithelium (RPE) of the eye.

57. A pharmaceutical composition comprising the rAAV of any one of claims 42-56, and a pharmaceutically acceptable carrier.

58. A kit for treating hearing loss and/or blindness, comprising the isolated nucleic acid of any one of claims 1-38, the vector of claims 39 or 40, or the rAAV of claims 42-56.

59. A method for treating hearing loss and/or vison loss in a subject in need thereof comprising:

administering to the subject an effective amount of the isolated nucleic acid of claims 1-38, or the rAAV of any one of claims 42-56.

60. The method of claim 59, wherein the subject is a mammal.

61. The method of claim 60, wherein the mammal is a human.

62. The method of claim 59 or 60, wherein the mammal is a non-human mammal.

63. The method of claim 62, wherein the non-human mammal is mouse, rat, or non-human primate.

64. The method of any one of claims 59-63, wherein the subject has or is suspected of having Usher Syndrome type 1F

65. The method of any one of claims 59-64, wherein the hearing loss and/or blindness is associated with Usher syndrome type 1F.

66. The method of any one of claims 59-65, wherein the hearing loss and/or blindness is associated with a mutation in the PCDH15 gene.

67. The method of claim 66, wherein the mutation of PCDH15 gene is a point mutation, a missense mutation, a nonsense mutation, a deletion, an insertion or a combination thereof.

68. The method of claim 67, wherein the subject is human; and the mutation is one or more mutations in Table 1.

69. The method of claims 67 or 68, wherein the subject is human; and the mutation comprises c.733C>T.

70. The method of any one of claims 59-69, wherein the mutation in the PCDH15 gene results in hearing loss and/or blindness.

71. The method of any one of claims 59-70, wherein the administration results in delivery of the isolated nucleic acid or rAAV to the ear or the eye of the subject.

72. The method of claim 71, wherein the administration results in delivery of the isolated nucleic acid or rAAV to the cochlea or the retina of the subject.

73. The method of any one of claims 72, wherein the administration is via injection.

74. The method of claim 73, wherein the injection is through round window membrane of the inner ear, or subretinal or intravitreal to the eye.

75. A method for correcting a point mutation of PCDH15 on a target sequence, comprising: contacting the target sequence with a base editor and a guide RNA.

76. A method for treating hearing loss and/or blindness in a subject in need thereof, comprising: administrating an effective amount of a base editor and a guide RNA, wherein the subject comprises a target sequence for a guide RNA.

77. The method of claim 76, wherein the hearing loss and/or blindness is associated with Usher Syndrome type 1F.

78. The method of claims 76 or 77, wherein the subject has or is suspected of having Usher Syndrome type 1F.

79. The method of any one of claims 75-78, wherein the base editor comprises (i) a nucleic acid programmable DNA binding protein (napDNAbp), (ii) a adenosine deaminase capable of deaminating adenine in deoxyribonucleic acid (DNA) and (iii) a linker between (i) and (ii).

80. The method of claim 79, wherein the nucleic acid programmable DNA binding protein (napDNAbp) is a Cas9 domain.

81. The method of claim 80, wherein the Cas9 domain is a nuclease dead Cas9 (dCas9) or a Cas9 nickase.

82. The method of anyone of claims 75-81, wherein the adenosine deaminase is derived from a bacterium.

83. The method of anyone of claims 82, wherein the adenosine deaminase is derived from *Escherichia coli.*

84. The method of anyone of claim 83, wherein the adenosine deaminase is derived from TadA protein of *Escherichia coli.*

85. The method of any one of claims 75-84, wherein the base editor comprises the amino acids sequences as set forth in any of SEQ ID NOs: 157, 159, 161, 163.

86. The method of any one of claims 75-85, wherein the point mutation of PCDH15 is associated with Usher syndrome type 1F.

87. The method of any one of claims 75-86, wherein the point mutation in PCDH15 is a point mutation.

88. The method of any one of claims 67, wherein the point mutation in PCDH15 is a point mutation in Table 1.

89. The method of claims 87 or 88, wherein the point mutation in PCDH15 is c. 733C>T.

90. The method of any one of claim 75-78, wherein the target sequence is in the genome of the subject.

91. The method of claim 90, wherein the subject is a mammal.

92. The method of claim 91, wherein the mammal is a human.

93. The method of claims 91, wherein the mammal is or a non-human mammal.

94. The method of any one of claims 75-93, wherein the guide RNA comprises a nucleic sequence at least 80% identical to nucleic acid sequence of SEQ ID NO: 51 and 165-172.

95. A kit for treating hearing loss and/or blindness, comprising:
(i) the base editor of any one of claims 75-94; and
(ii) the guide RNA of any one of claims 75-94.

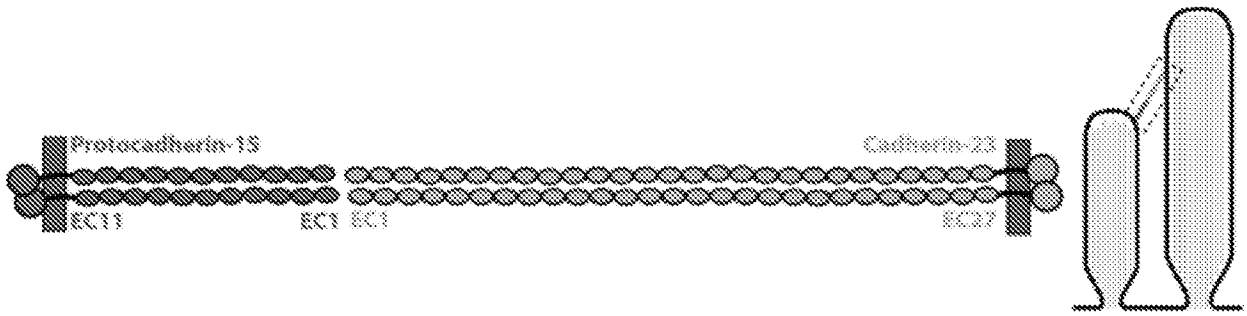

Protocadherin-15
Cadherin-23
EC11
EC1
EC1
EC27

FIG. 1A

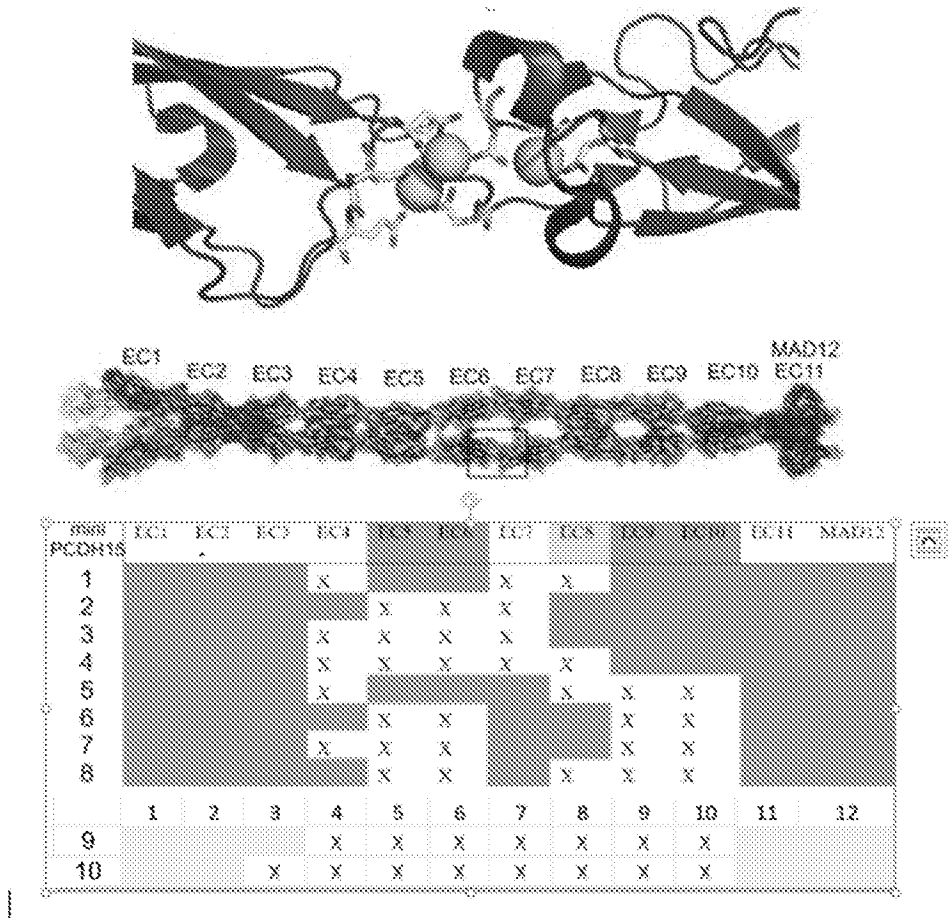

EC1
EC2
EC3
EC4
EC5
EC6
EC7
EC8
EC9
EC10
MAD12
EC11
PCDH15
1
2
3
4
5
6
7
8
9
10
1
2
3
4
5
6
7
8
9
10
11
12

FIG. 1B

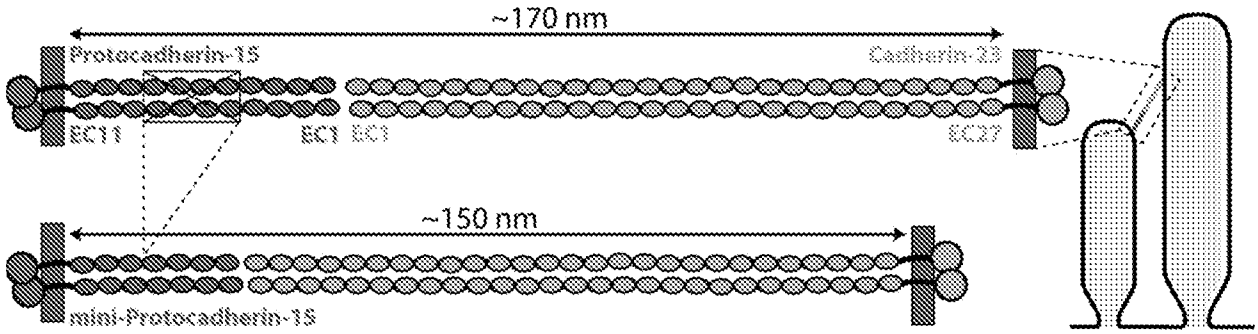

~170 nm
Protocadherin-15
Cadherin-23
EC11
EC1
EC3
EC27
~150 nm
mini-Protocadherin-15

FIG. 1C

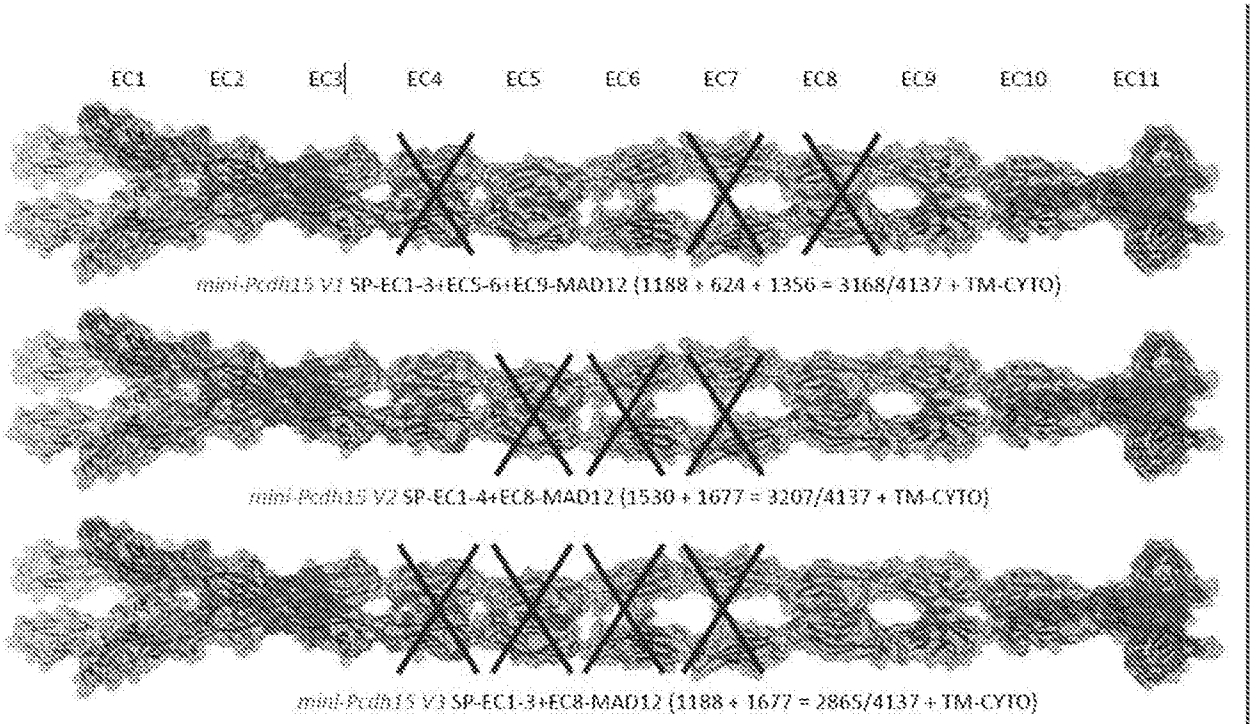

EC1
EC2
EC3
EC4
EC5
EC6
EC7
EC8
EC9
EC10
EC11
mini-Pcdh15 V1 SP-EC1-3+EC5-6+EC9-MAD12 (1188 + 624 + 1356 = 3168/4137 + TM-CYTO)
mini-Pcdh15 V2 SP-EC1-4+EC8-MAD12 (1530 + 1677 = 3207/4137 + TM-CYTO)
mini-Pcdh15 V3 SP-EC1-3+EC8-MAD12 (1188 + 1677 = 2865/4137 + TM-CYTO)

FIG. 1D

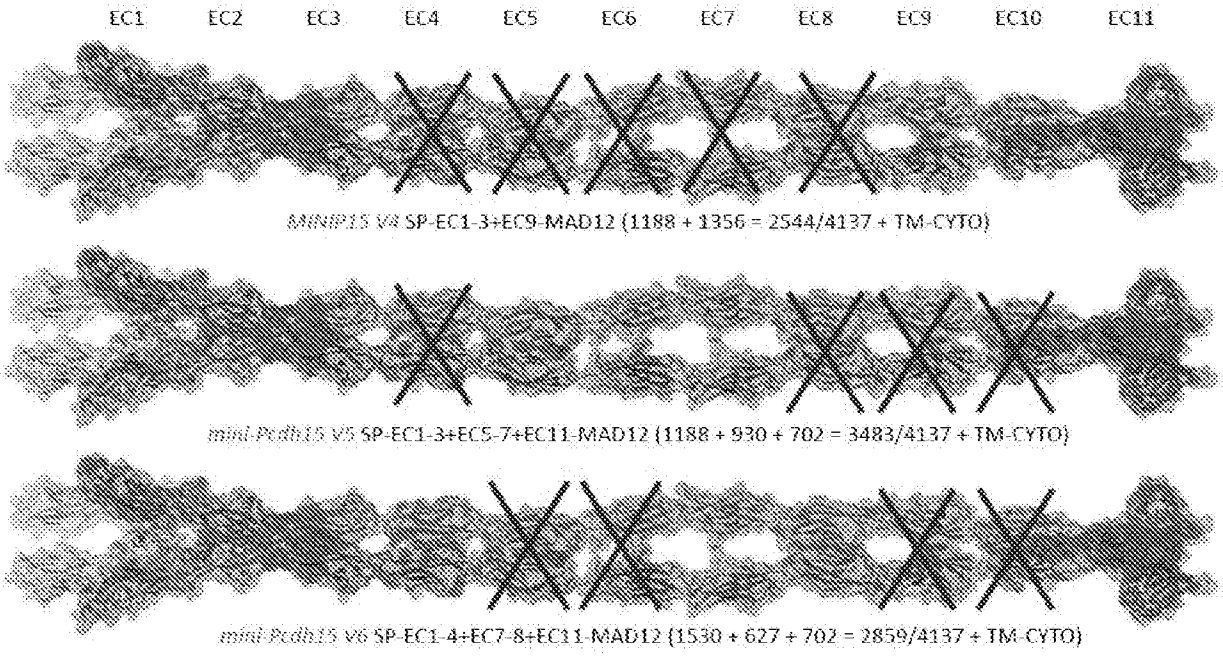

EC1
EC2
EC3
EC4
EC5
EC6
EC7
EC8
EC9
EC10
EC11
MINIP15 V4 SP-EC1-3+EC9-MAD12 (1188 + 1356 = 2544/4137 + TM-CYTO)
mini-Pcdh15 V5 SP-EC1-3+EC5-7+EC11-MAD12 (1188 + 930 + 702 = 3483/4137 + TM-CYTO)
mini-Pcdh15 V6 SP-EC1-4+EC7-8+EC11-MAD12 (1530 + 627 + 702 = 2859/4137 + TM-CYTO)

FIG. 1E

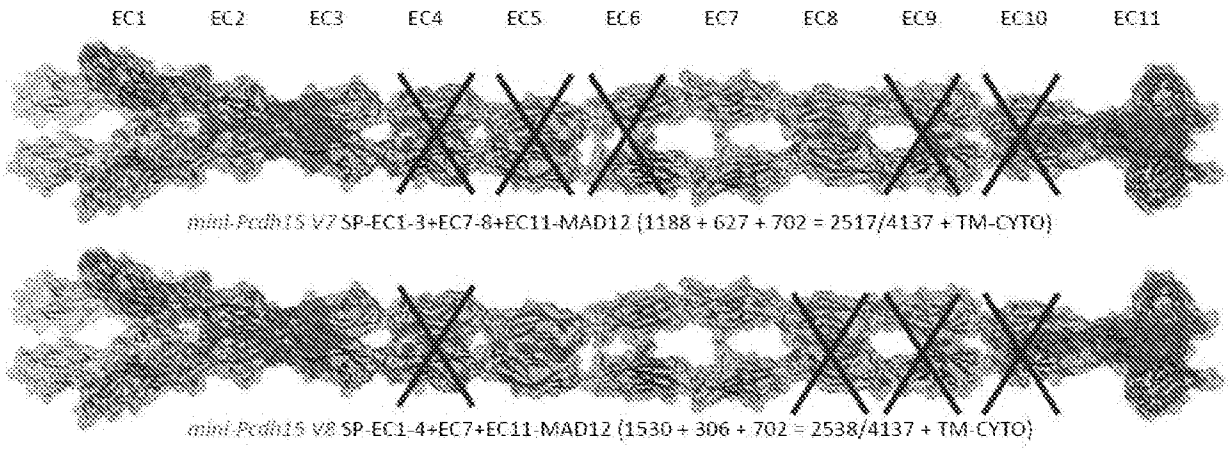

EC1
EC2
EC3
EC4
EC5
EC6
EC7
EC8
EC9
EC10
EC11
mini-Pcdh15 V7 SP-EC1-3+EC7-8+EC11-MAD12 (1188 + 627 + 702 = 2517/4137 + TM-CYTO)
mini-Pcdh15 V8 SP-EC1-4+EC7+EC11-MAD12 (1530 + 306 + 702 = 2538/4137 + TM-CYTO)

FIG. 1F

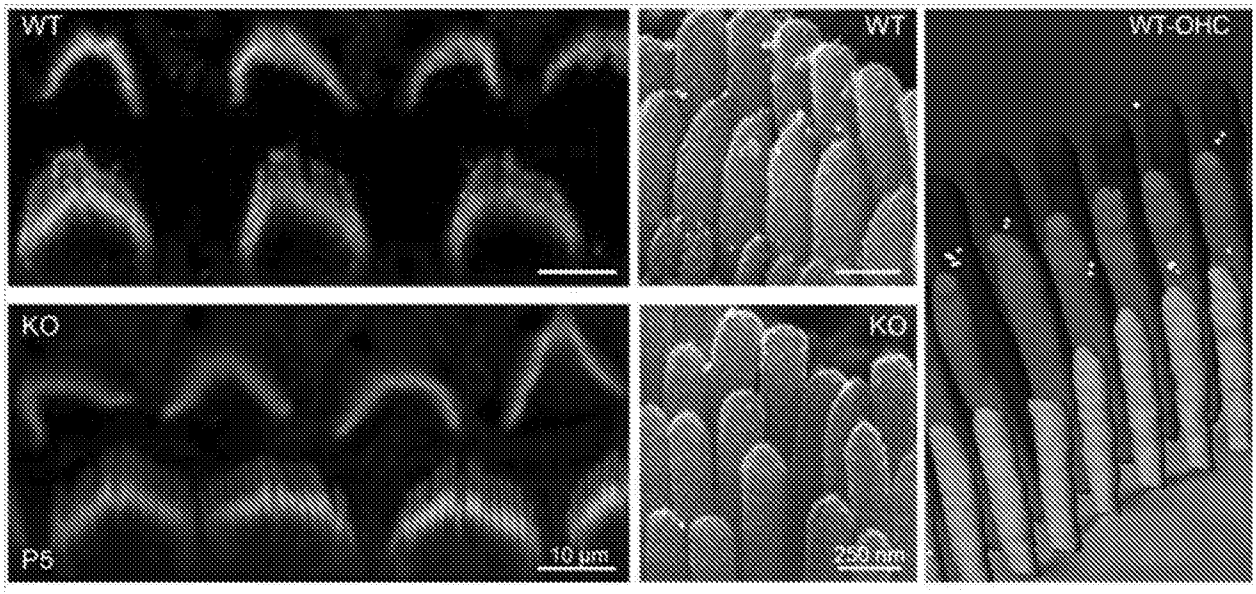

WT
WT
WT-GHC
KO
KO
P5
10 μm
250 nm

FIG. 1G

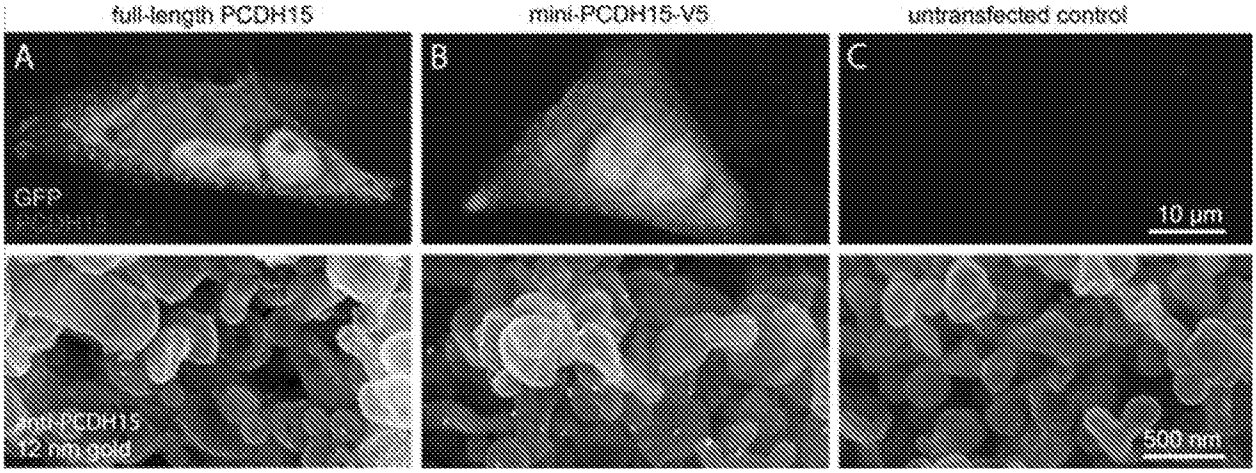

full-length PCDH15
mini-PCDH15-V5
untransfected control
A
B
C
GFP
10 μm
anti-PCDH15
12 nm gold
200 nm

FIG. 1H

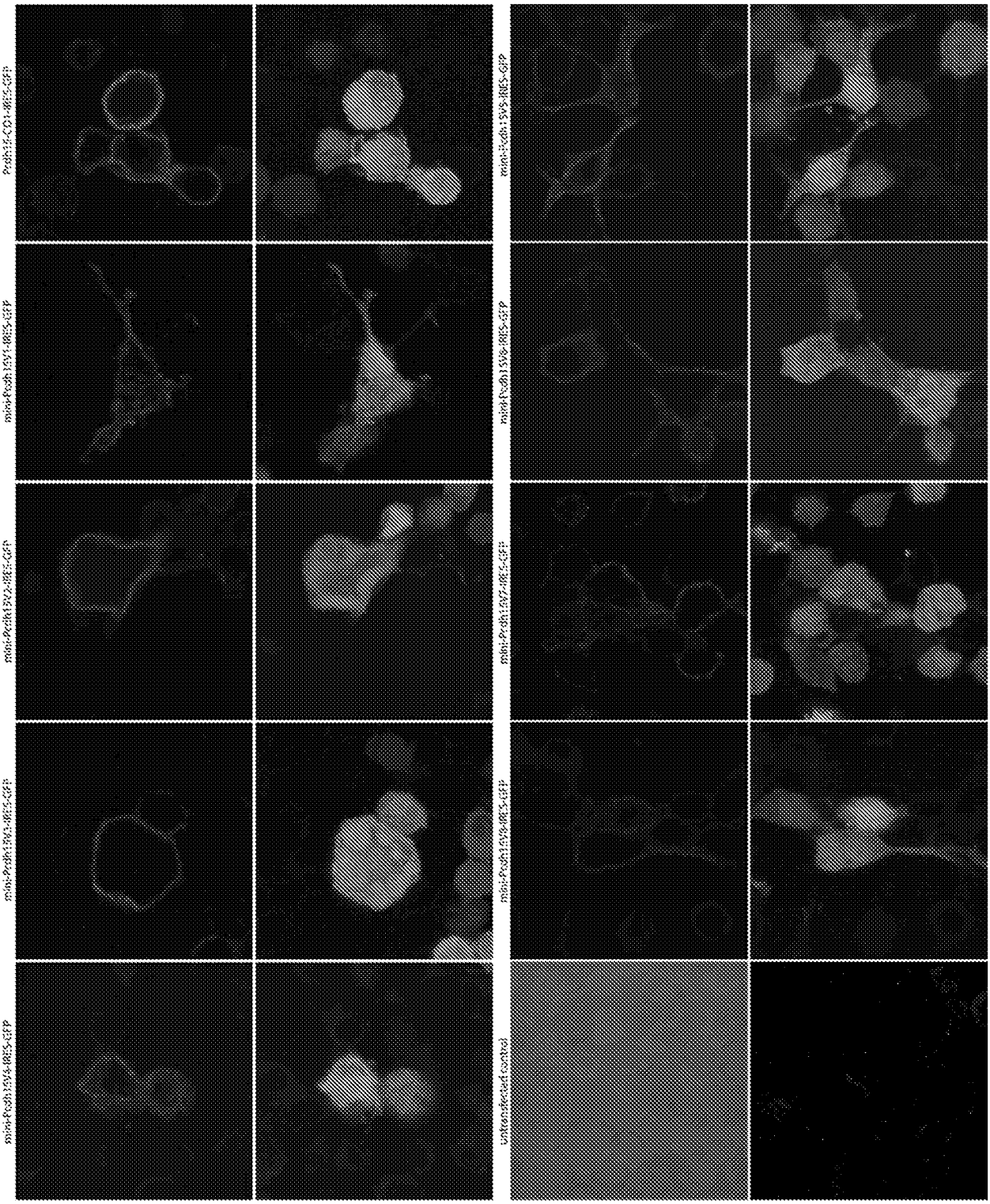

mini-Pcdh15CD1-IRES-GFP
mini-Pcdh15V5-IRES-GFP
mini-Pcdh15V6-IRES-GFP
mini-Pcdh15V7-IRES-GFP
mini-Pcdh15V8-IRES-GFP
mini-Pcdh15V4-IRES-GFP
untransfected control

FIG. 1I

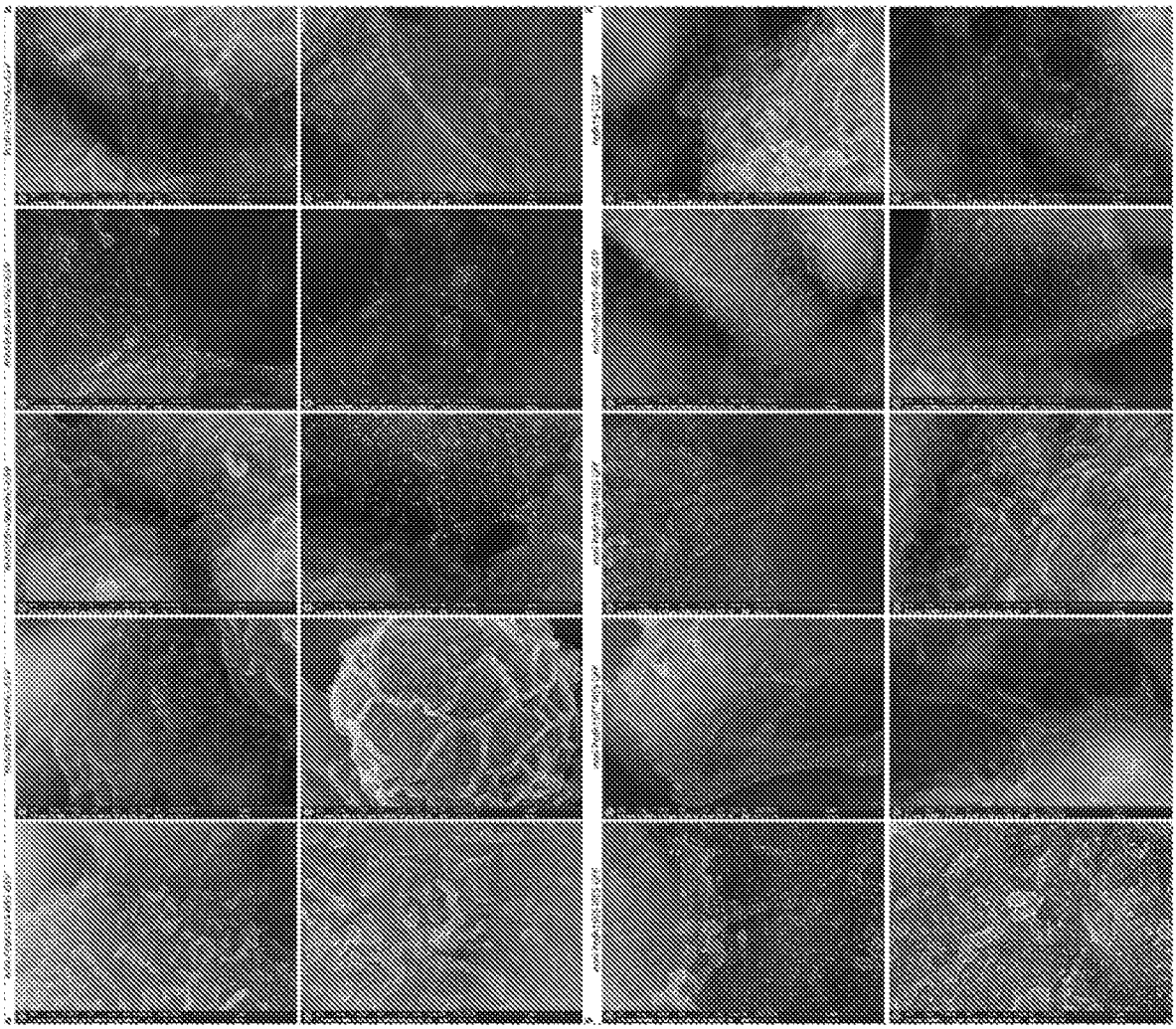


FIG. 1J

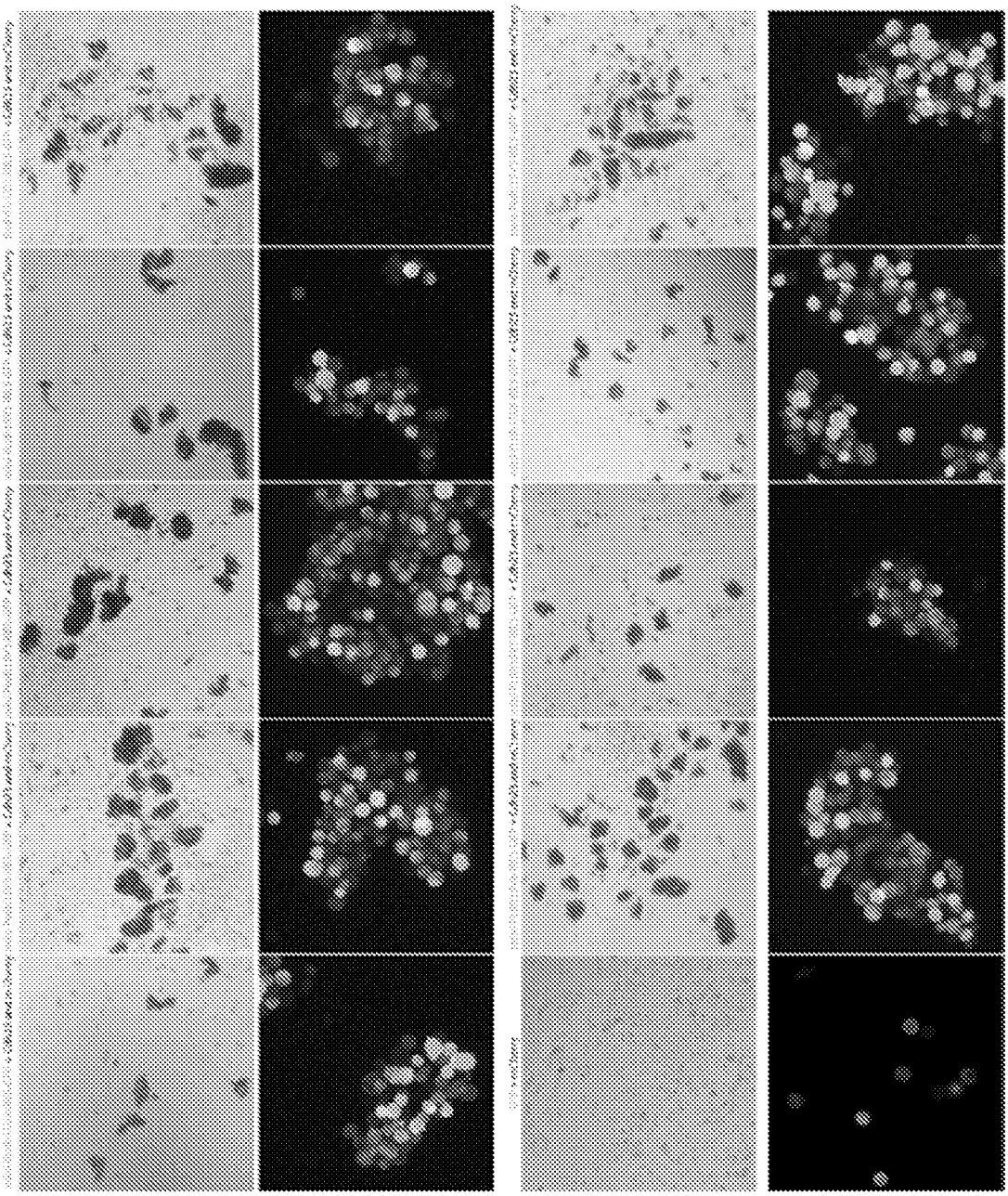


FIG. 1K

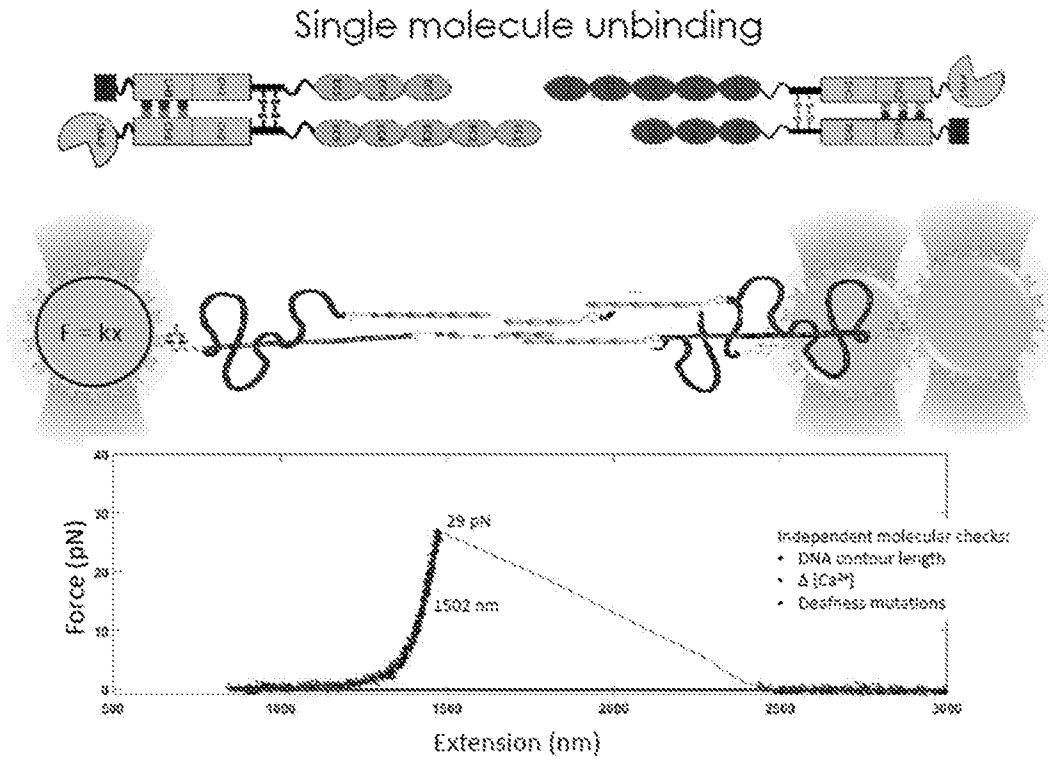

Single molecule unbinding
F = kx
29 pN
1502 nm
Force (pN)
Extension (nm)

FIG. 1L

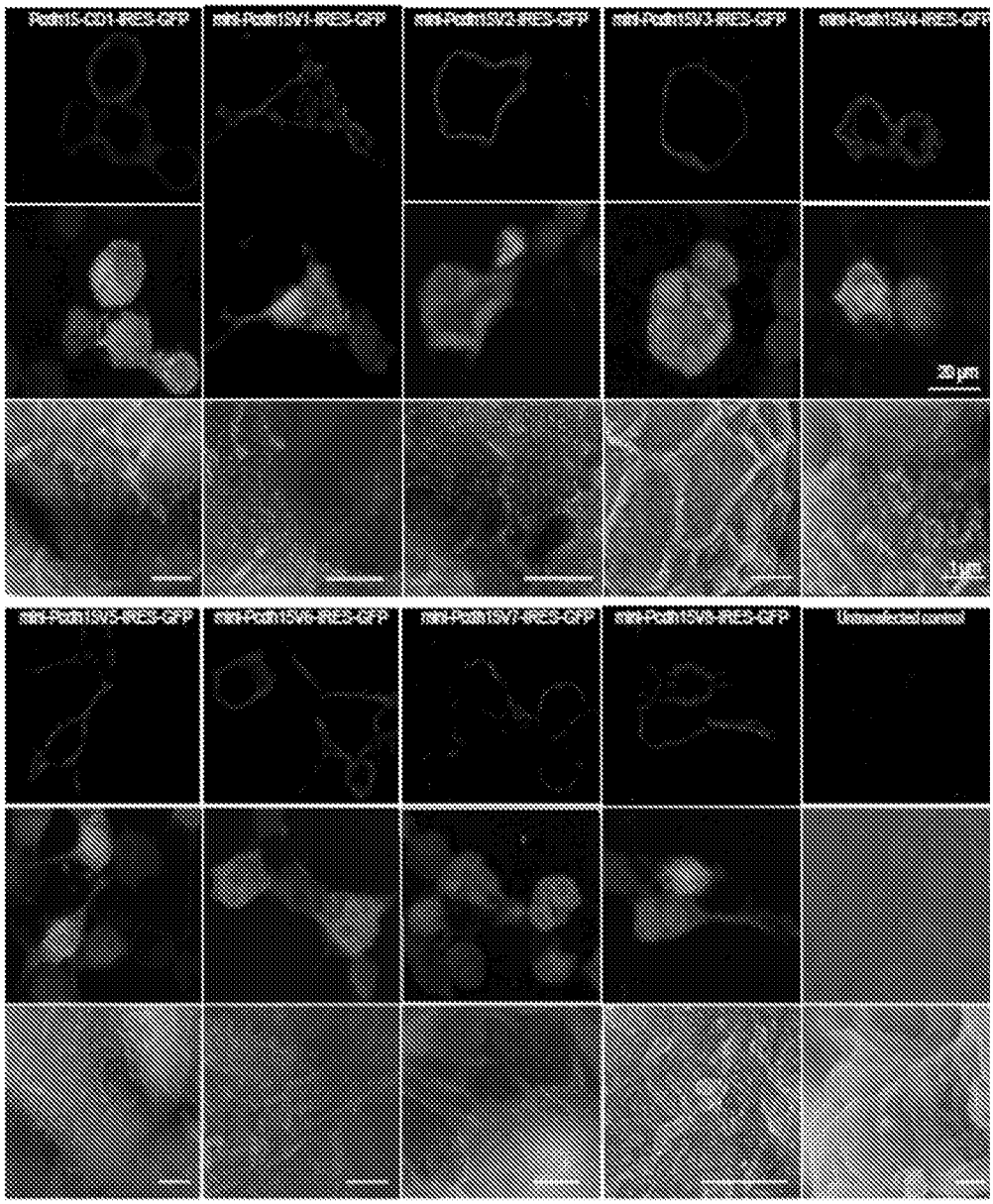


FIG. 1M

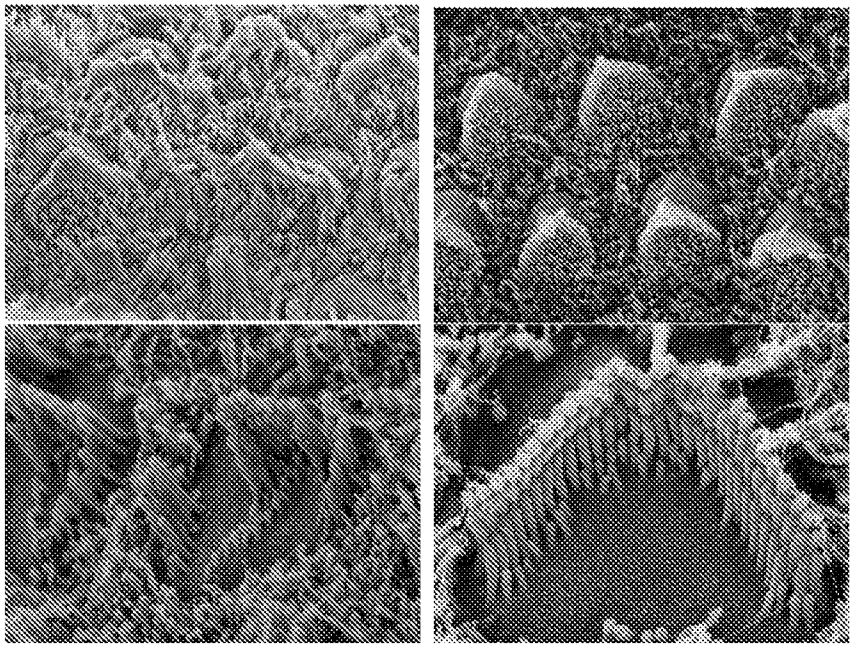


FIG. 1N

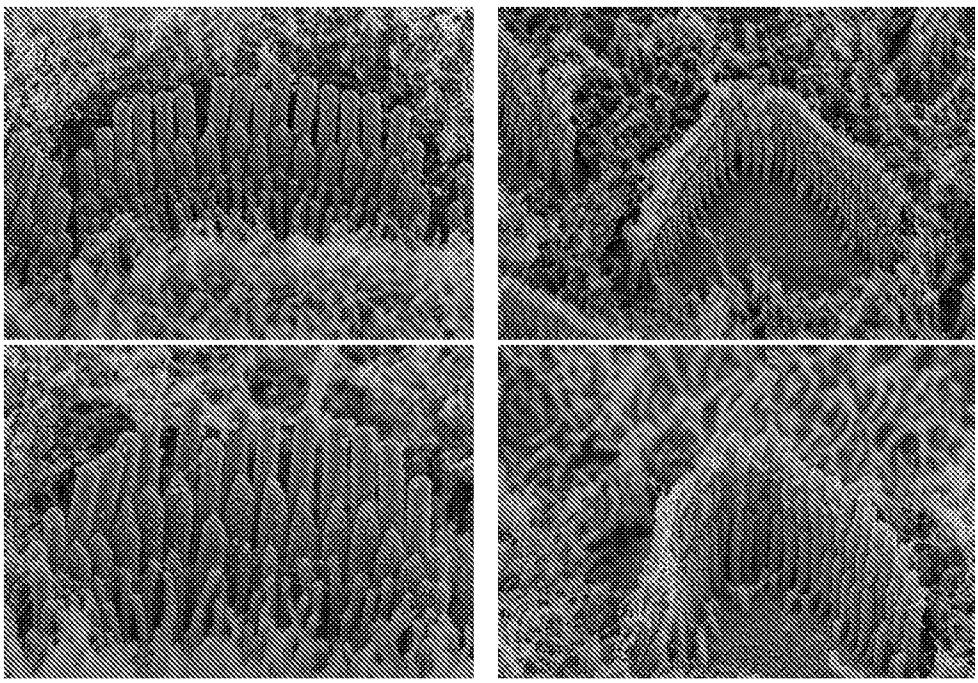


FIG. 1O

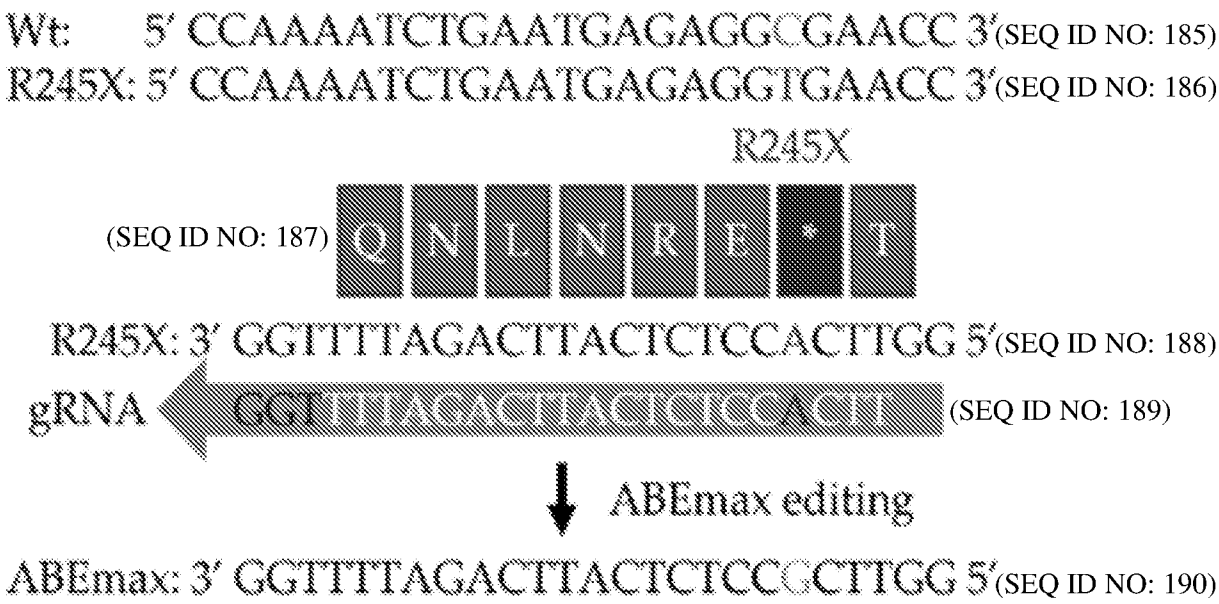

Wt: 5′ CCAAAATCTGAATGAGAGGCGAACC 3′ (SEQ ID NO: 185)
R245X: 5′ CCAAAATCTGAATGAGAGGTGAACC 3′ (SEQ ID NO: 186)
R245X
(SEQ ID NO: 187) Q N I N R E * I
R245X: 3′ GGTTTTAGACTTACTCTCCACTTGG 5′ (SEQ ID NO: 188)
gRNA GGTTTTAGACTTACTCTCCACTT (SEQ ID NO: 189)
ABEmax editing
ABEmax: 3′ GGTTTTAGACTTACTCTCCGCTTGG 5′ (SEQ ID NO: 190)

FIG. 2A

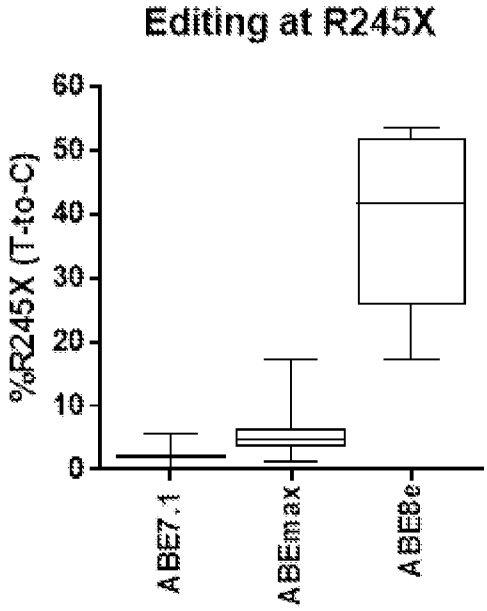

Editing at R245X
%R245X (T-to-C)
60
50
40
30
20
10
0
ABE7.1
ABEmax
ABE8e

FIG. 2B

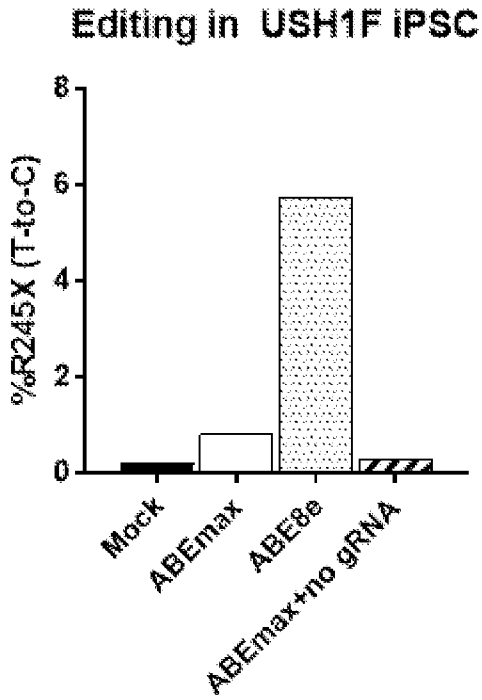

Editing in USH1F iPSC
%R245X (T-to-C)
8
6
4
2
0
Mock
ABEmax
ABE8e
ABEmax+no gRNA

FIG. 2C

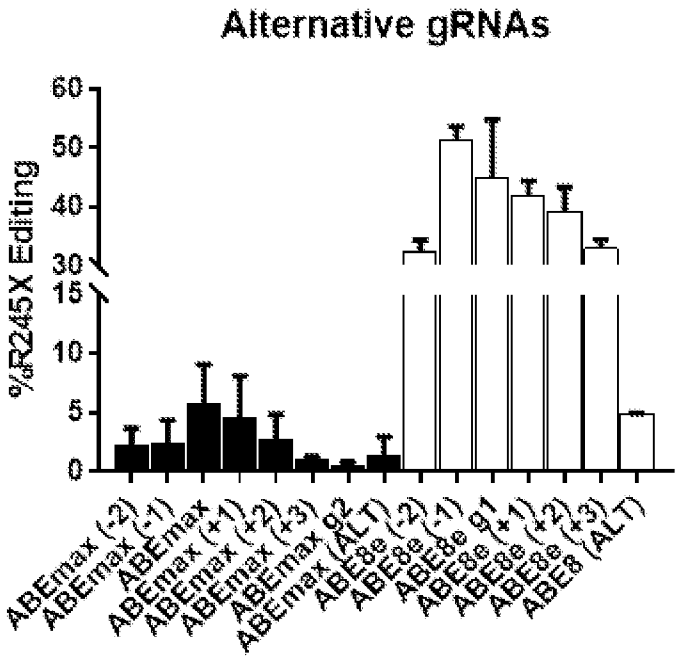

Alternative gRNAs
%R245X Editing
60
50
40
30
15
10
5
0
ABEmax (-2)
ABEmax (-1)
ABEmax
ABEmax (+1)
ABEmax (+2)
ABEmax (+3)
ABEmax 92
ABEmax (ALT)
ABE8e (-2)
ABE8e (-1)
ABE8e 91
ABE8e (+1)
ABE8e (+2)
ABE8e (+3)
ABE8 (ALT)

FIG. 2D

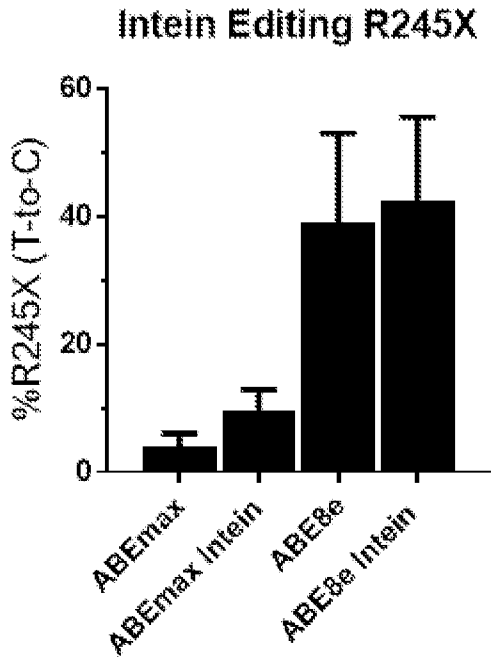

Intein Editing R245X
%R245X (T-to-C)
60
40
20
0
ABEmax
ABEmax Intein
ABE8e
ABE8e Intein

FIG. 2E

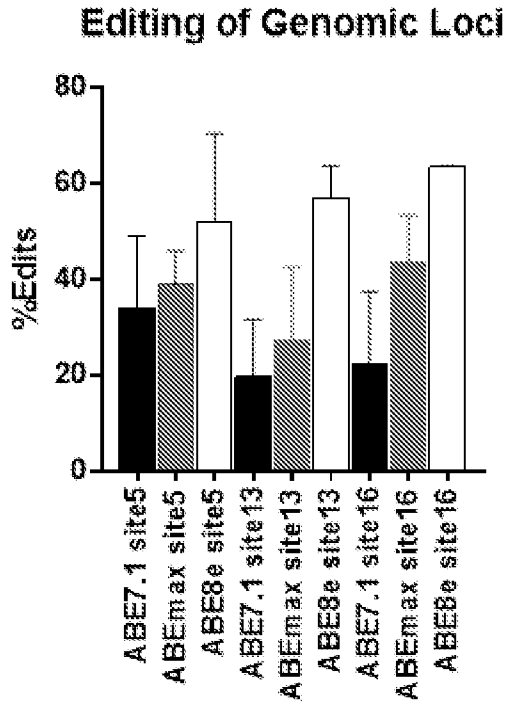

Editing of Genomic Loci
%Edits
80
60
40
20
0
ABE7.1 site5
ABEmax site5
ABE8e site5
ABE7.1 site13
ABEmax site13
ABE8e site13
ABE7.1 site16
ABEmax site16
ABE8e site16

FIG. 2F

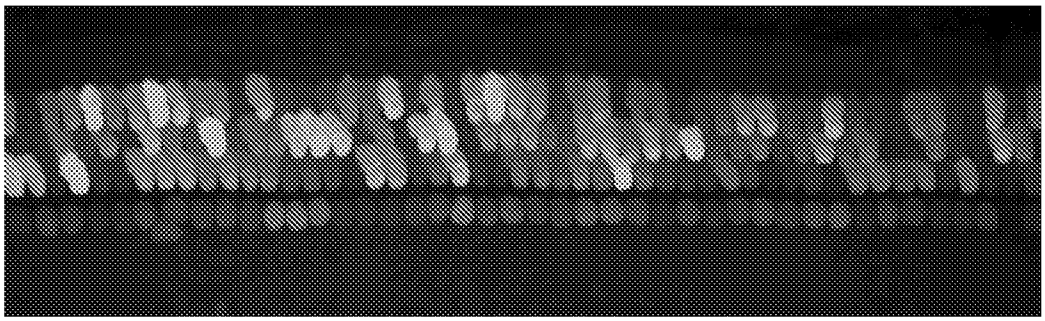


FIG. 3A

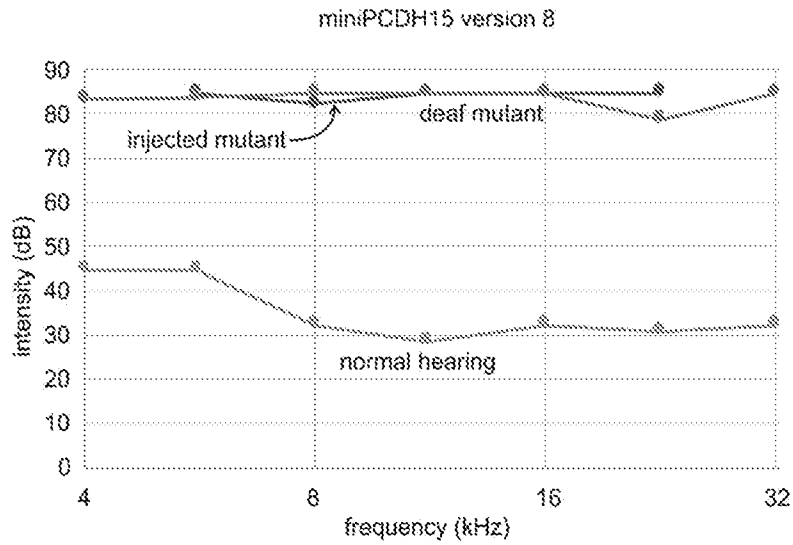

miniPCDH15 version 8
90
80
70
60
50
40
30
20
10
0
intensity (dB)
injected mutant
deaf mutant
normal hearing
4
8
16
32
frequency (kHz)

FIG. 3B

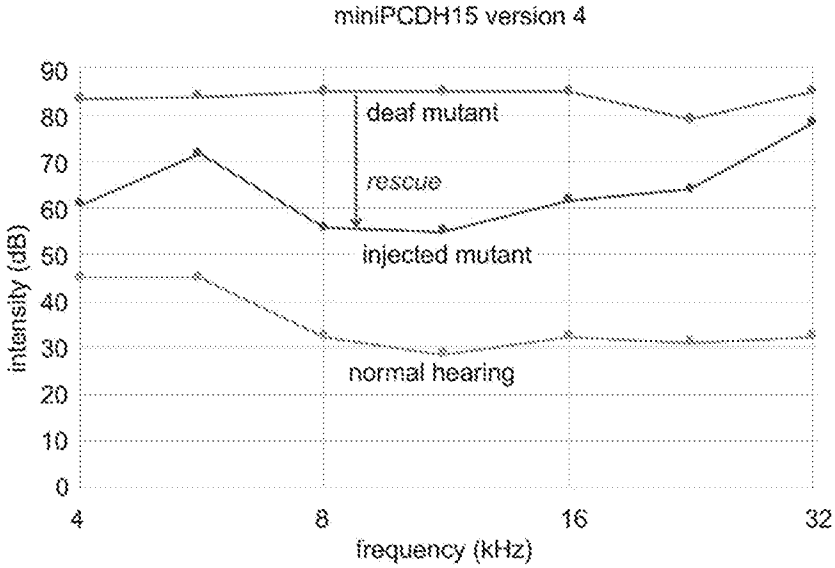

miniPCDH15 version 4
intensity (dB)
90
80
70
60
50
40
30
20
10
0
4
8
16
32
frequency (kHz)
deaf mutant
rescue
injected mutant
normal hearing

FIG. 3C

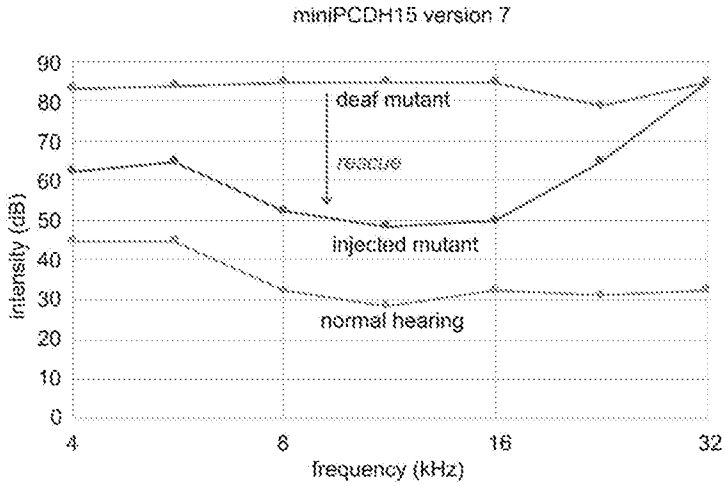

miniPCDH15 version 7
intensity (dB)
90
80
70
60
50
40
30
20
10
0
4
8
16
32
frequency (kHz)
deaf mutant
rescue
injected mutant
normal hearing

FIG. 3D

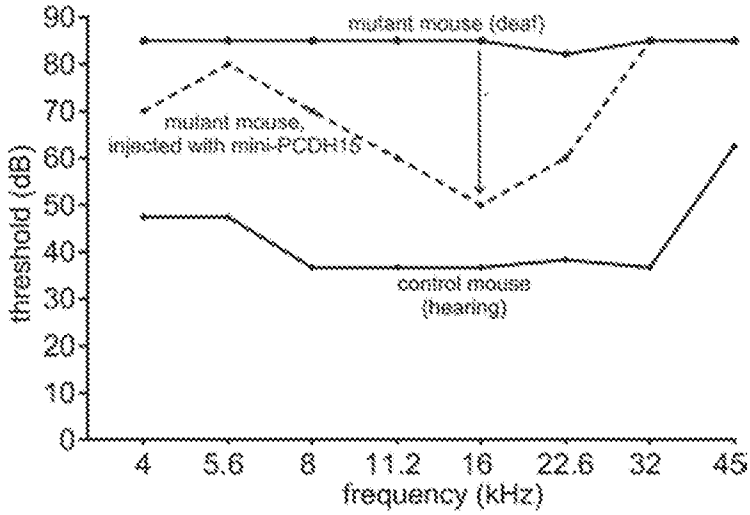

mutant mouse (deaf)
mutant mouse,
injected with mini-PCDH15
control mouse
(hearing)
threshold (dB)
90
80
70
60
50
40
30
20
10
0
4
5.6
8
11.2
16
22.6
32
45
frequency (kHz)

FIG. 3E

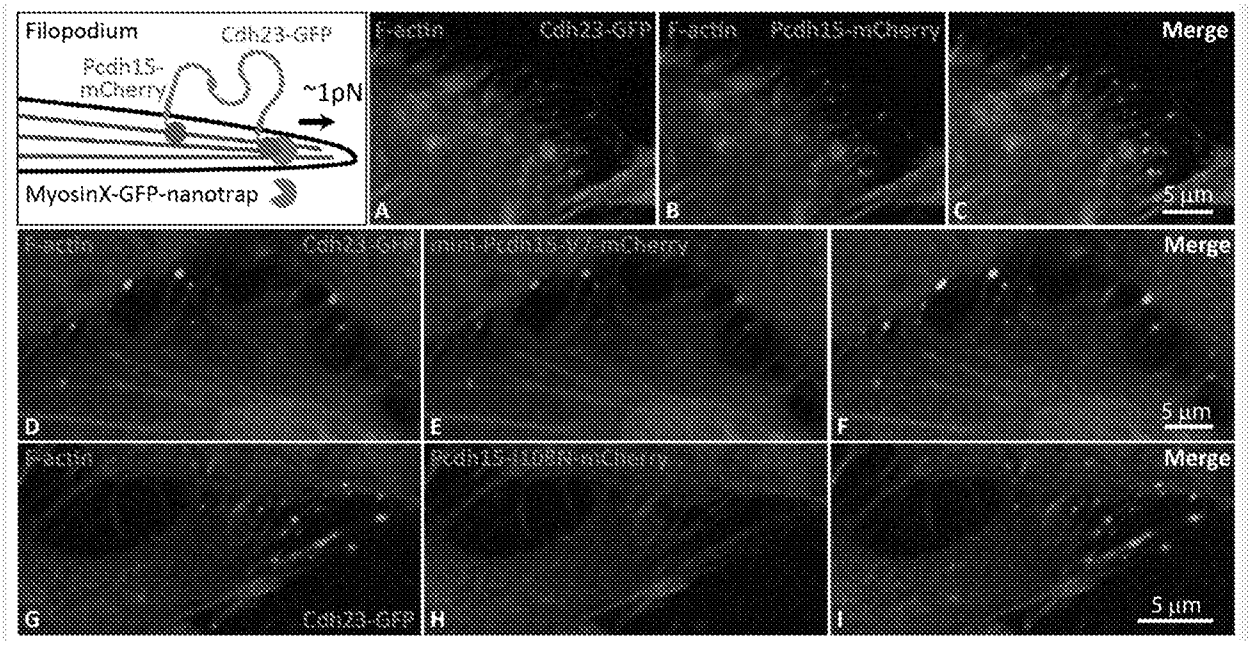

Filopodium
Cdh23-GFP
Pcdh15-mCherry
~1pN
MyosinX-GFP-nanotrap
F-actin
Cdh23-GFP
F-actin
Pcdh15-mCherry
Merge
A
B
C
5 μm
Merge
D
E
F
5 μm
Merge
G
Cdh23-GFP
H
I
5 μm

FIG. 4

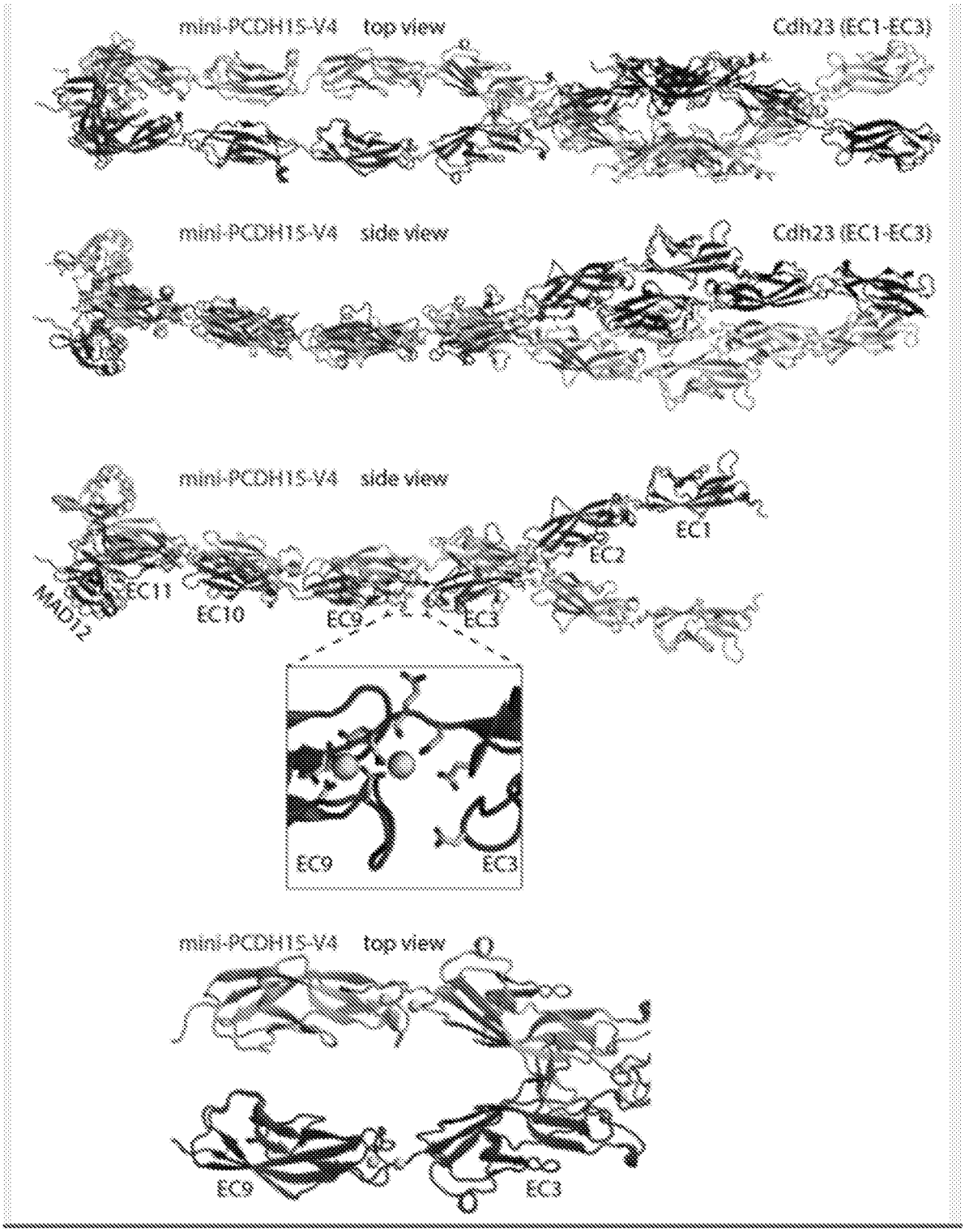

mini-PCDH15-V4 top view
Cdh23 (EC1-EC3)
mini-PCDH15-V4 side view
Cdh23 (EC1-EC3)
mini-PCDH15-V4 side view
EC1
EC2
EC3
EC9
EC10
EC11
MAD12
EC9
EC3
mini-PCDH15-V4 top view
EC9
EC3

FIG. 5A

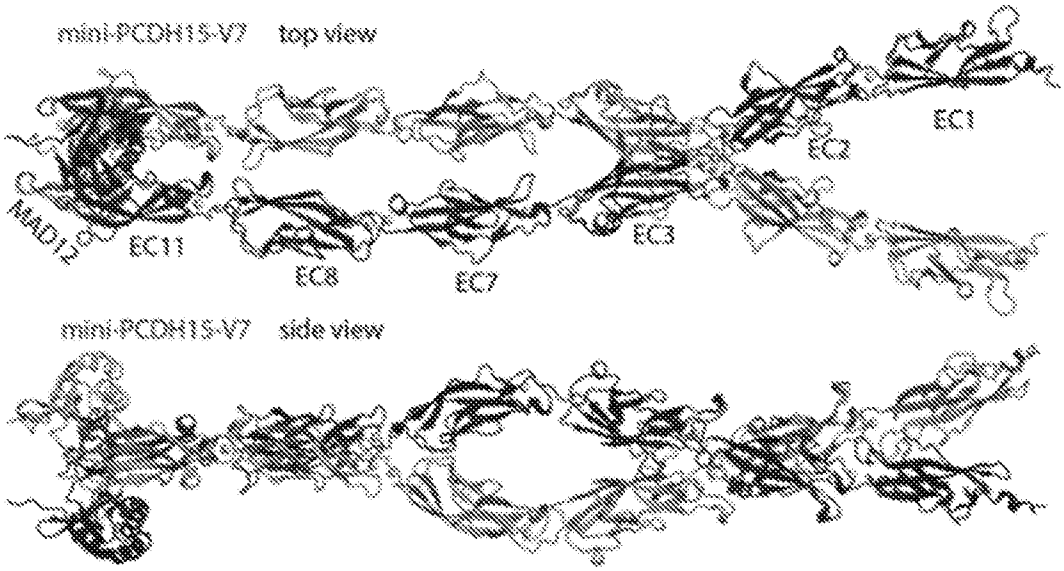

mini-PCDH15-V7 top view
EC1
EC2
EC3
EC7
EC8
EC11
MAD12
mini-PCDH15-V7 side view

FIG. 5B

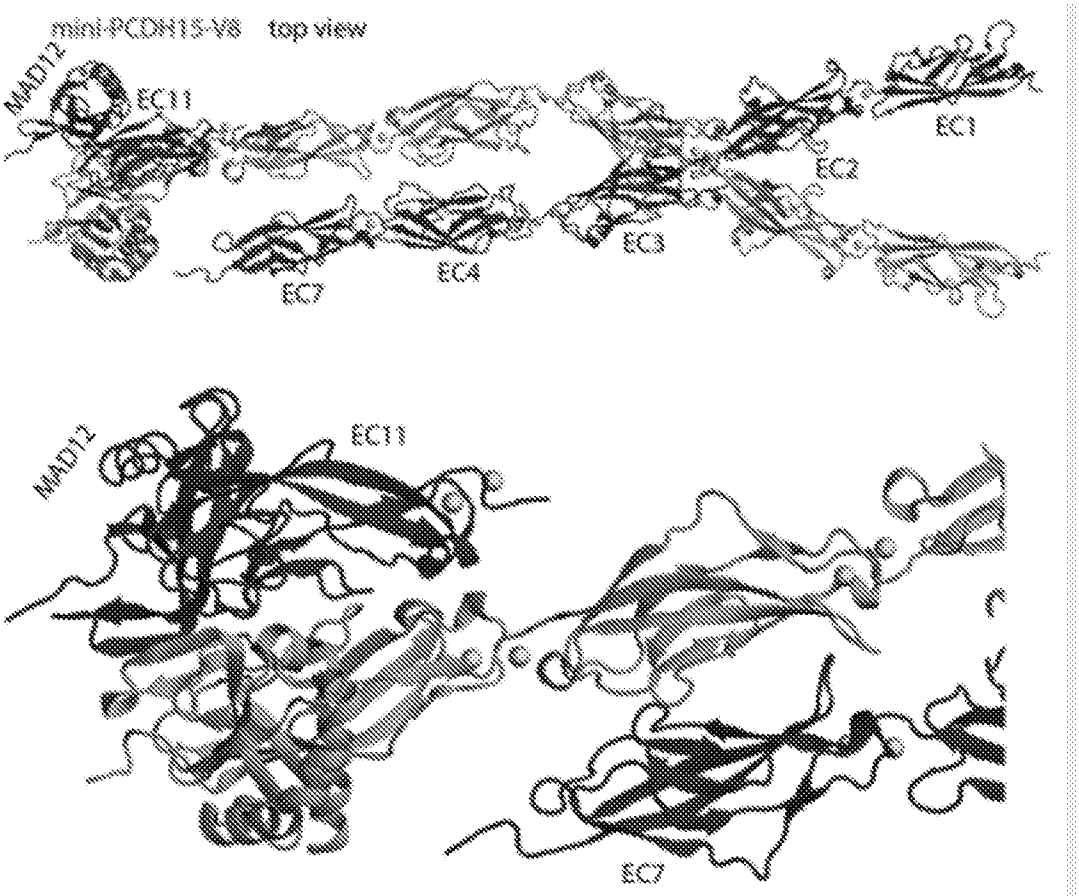

mini-PCDH15-V8 top view
MAD12
EC11
EC1
EC2
EC3
EC4
EC7
MAD12
EC11
EC7

FIG. 5C

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 20/29968

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C12N 15/86, C12N 9/22, C12N 15/85 (2020.01)

CPC - C12N 15/8645, C12N 15/861, C12N 15/8509, C12N 2310/20, C12N 2830/008

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 documont .

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.
X --- Y	WO 2018/145111 A1 (CHILDREN'S MEDICAL CENTER CORPORATION) 09 August 2018 (09.08.2018) pg 1, ln 29-30 - pg 2, ln 1; pg 11, ln 6-10; pg 12, ln 22-24; pg 13, ln 14-17; pg 14, ln 21-22; pg 35, ln5-7; Claim 1	1, 3/1 ------- 2, 3/2
Y	WO 2017/193059 A1 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA et al.) 09 November 2017 (09.11.2017) para [00110], [00330-00331]; Table 3; SEQ ID NO 1696	2, 3/2

☐ 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
28 August 2020	05 OCT 2020
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Lee Young Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 20/29968

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.: 4-74, 79-95
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:
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 searched, the appropriate additional search fees must be paid.

Group I: Claims 1-3, directed to an isolated nucleic acid comprising a mini-Protocadherin related 15 transgene flanked by adeno-associated virus inverted terminal repeats.

Group II: Claims 75-78, directed to a method for correcting a point mutation of PCDH15 on a target sequence.

----------Please see Supplemental Sheet----------

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.:
1-3

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
Information on patent family members

International application No.
PCT/US 20/29968

Continuation of Box No. III Observations where unity of invention is lacking:

The inventions listed as Groups I and II 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:

Special Technical Features

Group I requires an isolated AAV nucleic acid, not required by group II.

Group II requires method for correcting a point mutation of PCDH15 in a subject, not required by group I.

Common Technical Features

The common technical feature shared by Groups I and II that would otherwise unify the groups, is a nucleic acid comprising PCDH15 sequences.

However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is anticipated by WO 2018/145111 A1 to Children's Medical Center Corporation. (hereinafter "CMC"). CMC teaches an isolated nucleic acid (pg 13, ln 14-17 - "By "Isolated polynucleotide" is meant a nucleic acid (e.g., a DNA)...a recombinant DNA that is incorporated into a vector") encoding a mini-Protocadherin related 15 (mini-PCDH15) (pg 1, ln 29-30 - pg 2, ln 1 - "The invention provides compositions ... a transgene encoding a polypeptide of interest (e.g., TMC1, ... PCDH15)"; pg 14, ln 21-22 - "Nucleic acid molecules useful in the methods of the invention include any nucleic acid molecule that encodes a polypeptide of the invention or a fragment thereof.")

As the technical feature was known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the inventions

Groups I and II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Item 4, continued: claims 4-74, 79-95 are not not drafted in accordance with the second and third sentences of Rule 6.4(a) regarding multiply dependent claims.