

IMPROVED COMPOSITIONS AND METHODS FOR TREATMENT OF MONOGENIC NEURODEVELOPMENTAL DISORDERS

Technical Field

- 5 The present disclosure generally is directed to oligonucleotides and related compositions and methods for treating conditions associated with mutations in the *SHANK3* gene.

Background

- 10 SHANK3 is a widely expressed scaffolding protein enriched in the post-synaptic density of excitatory synapses in the brain. SHANK3 recruits and stabilizes ionotropic and metabotropic glutamate receptors (AMPA, NMDA, mGluR) to the post-synaptic density. *SHANK3* gene mutations/deletions and SHANK3 haploinsufficiency underlie the rare genetic neurodevelopmental disorder, Phelan-McDermid syndrome, and have
15 been attributed to 0.5%-1% of autism spectrum disorders (ASD), 2% of intellectual disability diagnoses, and 0.6%-2.16% of atypical schizophrenia diagnoses.

- Phelan-McDermid syndrome is characterized by intellectual disability of varying degrees, neonatal hypotonia, absent to severely delayed speech development, moderate to profound developmental delay, motor regression and minor dysmorphic features.
20 Approximately 14-70% of affected individuals develop seizures ranging from mild to severe. Other complications include kidney abnormalities, gastrointestinal issues, reduced perspiration and risk of overheating, lack of perception of pain, arachnoid cysts, or other comorbid neuropsychiatric illnesses. Children are typically diagnosed in early childhood, often due to significant delays in reaching early developmental milestones.
25 There is currently no effective treatment for conditions caused by SHANK3 haploinsufficiency such as Phelan-McDermid syndrome. Thus, there is an ongoing need to provide effective compositions and methods for treating such conditions.

Summary

The *SHANK3* gene includes 22 exons spanning 58 kb of genomic DNA on the terminal end of chromosome 22 (22q13 region) and its major protein product is a 1,607 amino acid polypeptide. There are at least six known isoforms that are temporally and spatially specific and have distinct functions at the synapse. *SHANK3* contains five protein-protein interaction domains, and each isoform contains distinct combinations of these five domains.

While not wishing to be bound by theory, *SHANK3* haploinsufficiency due to loss of function gene mutation(s), including nonsense, missense and frameshift mutations, as well as partial or whole gene deletions, results in insufficient protein production.

The present disclosure provides antisense oligonucleotides (ASO), antisense RNA (AR) expression vectors, and related compositions and methods to increase *SHANK3* protein levels by modulating the stability of *SHANK3* mRNA to increase the level of *SHANK3* mRNAs encoding functional *SHANK3* isoforms. Also disclosed are methods for treating conditions associated with *SHANK3* haploinsufficiency.

Accordingly, in one aspect provided herein is an antisense oligonucleotide that binds within a targeted portion of the 3' UTR of a *SHANK3* mRNA (**SEQ ID NO:1**); whereby binding of the antisense oligonucleotide within the targeted portion in a mammalian cell results in an increased level of *SHANK3* protein in the mammalian cell. In some examples the targeted portion comprises the sequence according to **SEQ ID NO:1079**. In some examples the targeted portion consists of the sequence according to **SEQ ID NO:1079**.

In a related aspect provided herein is vector for expression, in a mammalian neuron, of an antisense RNA (AR) that binds within a targeted portion of the 3' UTR of a *SHANK3* mRNA; whereby binding of the AR within the targeted portion in a mammalian cell results in an increased level of *SHANK3* protein in the mammalian cell.

In some examples the sequence of the *SHANK3* mRNA 3' UTR comprises the sequence corresponding to **SEQ ID NO:1**. In some examples the targeted portion

comprises the sequence according to **SEQ ID NO:1079**. In some examples the targeted portion consists of the sequence according to **SEQ ID NO:1079**.

In some examples the nucleotide sequence of the ASO or AR is at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% complementary to the nucleotide
5 sequence of the targeted portion over the length of the ASO or the AR.

In some examples the mammalian cell in which a SHANK3 level is increased is a neuron.

In some examples the vector includes a neuron-selective promoter for driving expression of the AR in the mammalian neuron. In some examples the neuron-selective
10 promoter is selective for expression in a neuron type selected from the list consisting of: cortical, striatal, cerebellar and hippocampal excitatory or inhibitory neurons, including, but not limited to cortical glutamatergic neurons, cortical GABAergic neurons, hippocampal glutamatergic neurons, and striatal inhibitory neurons. In some examples the vector includes an inducible promoter. In some examples the vector is a non-viral
15 vector. In some examples a non-viral vector further comprises a transfection agent. In other examples the vector is a viral vector. In some examples, where the vector is a viral vector, the viral vector is a recombinant virus selected from the group consisting of: adeno-associated virus (AAV), adenovirus, lentivirus, and anellovirus.

In some examples the nucleotide sequence of the ASO or AR comprises up to two
20 base mismatches to the targeted portion.

In some examples the nucleotide sequence of the ASO or AR corresponds to any one of **SEQ ID NOs:1080-1093**.

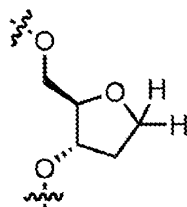
In some examples the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1080-1093** or **1096-1133**. In some examples the nucleotide sequence of
25 the ASO corresponds to any one of **SEQ ID NOs:1080-1093**. In some examples the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1084, 1087, or 1091-1093**. In some examples the nucleotide sequence of the ASO corresponds to **SEQ ID NO:1084**. In some examples the nucleotide sequence of the ASO corresponds to **SEQ ID NO:1087**. In some examples the nucleotide sequence of the ASO corresponds
30 to **SEQ ID NO:1091**. In some examples the nucleotide sequence of the ASO

corresponds to **SEQ ID NO:1092**. In some examples the nucleotide sequence of the ASO corresponds to **SEQ ID NO:1093**.

In some examples the nucleotide sequence of the ASO or AR corresponds to any one of **SEQ ID NOs:1096-1133**. In some examples the nucleotide sequence of the ASO or AR corresponds to any one of **SEQ ID NOs:1096, 1109, 1119, and 1128**. In some examples the nucleotide sequence of the ASO corresponds to **SEQ ID NO:1096**. In some examples the nucleotide sequence of the ASO corresponds to **SEQ ID NO:1109**. In some examples the nucleotide sequence of the ASO corresponds to **SEQ ID NO:1119**. In some examples the nucleotide sequence of the ASO corresponds to **SEQ ID NO:1128**.

10 In some examples any of the foregoing ASOs include a backbone modification. In some examples the backbone modification includes a phosphorothioate linkage or a phosphorodiamidate linkage. In other examples the ASO includes a phosphorodiamidate morpholino, an arabinonucleic acid, a locked nucleic acid, a peptide nucleic acid, a 2'-O- modification such as a 2'-O-methyl, a 2'-Fluoro, or a 2'-O-methoxyethyl moiety, or

15 an abasic spacer subunit. In some examples the abasic spacer subunit comprises the structure according to Formula I:



Formula I

In some examples the nucleotide sequence of the ASO comprises one or more abasic spacer subunits and/or locked nucleic acids. In some examples the nucleotide sequence of the ASO comprises one or more abasic spacer subunits and one or more locked nucleic acids. In some examples, where the ASO comprises at least one abasic spacer subunit, at least one locked nucleic acid, or both, the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1096-1133**. In some examples the nucleotide sequence of the ASO or AR targeting the 3' UTR corresponds to any one of

20 **SEQ ID NOs:3-1133, SEQ ID NOs:1134-4583, and SEQ ID NOs:16254-18750**.

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In some examples the ASO includes at least one modified sugar moiety. In other examples each sugar moiety in the ASO is a modified sugar moiety. In some examples the ASO includes a 2'-*O*-methoxyethyl moiety. In other examples each nucleotide of the ASO includes a 2'-*O*-methoxyethyl moiety.

5 In some examples of any of the foregoing ASOs or vectors, the nucleotide sequence of the ASO or AR is 10 to 50 nucleotides, 15 to 40 nucleotides, 17 to 30 nucleotides, 15 to 30 nucleotides, 18 to 40 nucleotides, 17 to 25 nucleotides, 20 to 35 nucleotides, 15 to 30 nucleotides, 20 to 30 nucleotides, 22 to 30 nucleotides, 24 to 30 nucleotides, 25 to 30 nucleotides, or 26 to 30 nucleotides in length. In some examples,
10 where the ASO is 17 to 30 nucleotides in length, the ASO includes one or more phosphorodiamidate morpholino moieties. In other examples, where the ASO is 15 to 30 nucleotides in length, the ASO includes one or more phosphorodiamidate morpholino moieties.

In some examples any of the foregoing ASOs are linked to a functional moiety.
15 In some examples the functional moiety includes a delivery moiety. In some examples the delivery moiety is selected from the group consisting of: lipids, polyethers, peptides, carbohydrates, receptor binding peptide (RBP), and antibodies. In some examples, wherein the ASO includes a delivery moiety, the delivery moiety includes a cell-penetrating peptide (CPP). In some examples the CPP comprises the amino acid
20 sequence corresponding to **SEQ ID NO:2**. In some examples the delivery moiety includes a *N*-acetylgalactosamine (GalNAc) or glycan moiety. In some examples the delivery moiety includes a fatty acid or lipid moiety. In some embodiments the fatty acid chain length is about C8 to C20. In other examples the functional moiety includes a stabilising moiety. In some examples the functional moiety is covalently linked to the
25 ASO. In other examples the functional moiety is non-covalently linked to the ASO. In some examples the functional moiety is linked to the 5' end of the ASO. In other examples the functional moiety is linked to the 3' end of the ASO. In some examples any of the foregoing ASOs also include a delivery nanocarrier, wherein the nanocarrier is complexed with the ASO. In some examples the delivery nanocarrier is selected from
30 the group consisting of: lipoplexes, liposomes, exosomes, inorganic nanoparticles, and

DNA nanostructures. In some examples the delivery nanocarrier includes a lipid nanoparticle (LNP) encapsulating the ASO.

In a related aspect provided herein is a pharmaceutical composition that includes any of the foregoing ASOs, vectors, or compositions and a pharmaceutically acceptable
5 excipient. In some preferred embodiments the pharmaceutical composition comprises an ASO as disclosed herein. In some embodiments the pharmaceutical composition is provided as a gymnotic formulation of the ASO (*i.e.*, a formulation devoid of agents to facilitate transfection of the ASO).

In a further related aspect provided herein is a method for preventing or treating
10 a condition associated with SHANK3 haploinsufficiency, the method comprising administering to a subject in need thereof a therapeutically effective amount of the foregoing pharmaceutical composition. In some examples the condition to be treated is Phelan-McDermid syndrome, an autism spectrum disorder, schizophrenia, or an intellectual disability. In some examples the condition to be treated is Phelan-McDermid
15 syndrome. In some examples the subject to be treated is a human subject.

In a further aspect provided herein is the use of any of the foregoing antisense oligonucleotides or vectors in the manufacture of a medicament for prevention or treatment of a condition associated with SHANK3 haploinsufficiency.

In some examples of the foregoing methods of treatment or uses, the level of
20 SHANK3 protein in at least a plurality of cells in the subject is increased about 1.1 to about 5 fold in cells (*e.g.*, neurons) *in vitro* or *ex vivo*, *e.g.*, 1.2 fold, 1.3 fold, 1.5 fold, 1.7 fold, 2 fold, 2.2 fold, 2.5 fold, 2.7 fold, 3 fold, 3.3 fold, 3.5 fold, 4 fold, 4.3 fold, 4.5 fold, 4.7 fold, or another increase in SHANK3 protein levels from about 1.1 fold to about 5 fold in cells in a subject compared to the level in the absence of the pharmaceutical
25 composition.

In some examples of the foregoing methods of treatment or uses, the ratio of the levels of SHANK3 protein essential isoforms relative to each other following the treatment are unchanged.

In yet another aspect provided herein is a genetically modified cell comprising
30 any of the foregoing ASOs or vectors. In some examples the genetically modified cell is a mammalian cell. In some examples the genetically modified mammalian cell is a

human cell. In some examples the genetically modified mammalian cell is a genetically modified neuron or neural progenitor. In some examples, the genetically modified neuron is selected from the group consisting of: cortical, striatal, cerebellar and hippocampal excitatory or inhibitory neurons, including, but not limited to cortical
5 glutamatergic neurons, cortical GABAergic neurons, hippocampal glutamatergic neurons, and striatal inhibitory neurons. In some examples the genetically modified neuron is a cortical glutamatergic neuron obtained by differentiation of an hiPSC line, wherein the hiPSC line is derived from a subject suffering from Phelan-McDermid syndrome or a subject not suffering from Phelan-McDermid syndrome. In some
10 embodiments the genetically modified mammalian cell is not a human embryonic cell. In some examples the genetically modified mammalian cell is from a cell line. In some examples the cell line is a human induced pluripotent stem cell (hiPSC) line or a cell line derived from neurons.

In other examples the level of SHANK3 can be increased by modulating splicing
15 (including alternative splicing) of *SHANK3* pre-mRNA transcripts. The term alternative splicing refers to a process whereby exons, or part of an exon of a gene, or introns or part of an intron may be included within or excluded from the final mRNA transcript. Mature noncanonical mRNA transcripts can be non-productive due to a frame shift that may induce the nonsense mediated decay pathway. In other cases, translation of the
20 noncanonical mRNA can produce a truncated but non-functional protein. Alternative splicing of the *SHANK3* pre-RNA transcripts can downregulate overall *SHANK3* mRNA and protein expression.

Introns are removed by a large RNA-protein complex termed the spliceosome, which orchestrates complex interactions between primary transcripts, small nuclear
25 RNAs (snRNAs) and a large number of proteins. Spliceosomes assemble on each intron in an ordered manner, starting with recognition of the 5' splice site (5' ss) by U1 snRNA or the 3' splice site (3' ss) by the U2 pathway, which involves binding of the U2 auxiliary factor (U2AF) to the 3' ss region to facilitate U2 binding to the branch point sequence (BPS). U2AF is a stable heterodimer composed of a U2AF2-encoded 65-kD subunit
30 (U2AF65), which binds the polypyrimidine tract (PPT), and a U2AF1-encoded 35-kD subunit (U2AF35), which interacts with highly conserved AG dinucleotides at 3' ss and

stabilizes U2AF65 binding. In addition to the BPS/PPT unit and 3' ss/5' ss, accurate splicing requires auxiliary sequences or structures that activate or repress splice site recognition, known as intronic or exonic splicing enhancers or silencers. These elements allow genuine splice sites to be recognized among a vast excess of cryptic or pseudo-sites in the genome of higher eukaryotes, which have the same sequences but outnumber authentic sites by an order of magnitude.

In some examples the present disclosure provides antisense oligonucleotides (ASO), antisense RNA (AR) expression vectors, and related compositions and methods to increase SHANK3 protein levels. While not wishing to be bound by theory, it is believed that in some examples ASOs effect an increase in SHANK3 protein levels by modulating splicing of SHANK3 mRNA to increase the level of canonical SHANK3 mRNA encoding full length, functional SHANK3. More specifically, it is believed that the ASOs modulate splicing to decrease aberrant intron retention, particularly any one of introns 6, 7, 16, 17, 18, or 20. Also disclosed are methods for treating conditions associated with SHANK3 haploinsufficiency.

Accordingly, in one aspect provided herein is an antisense oligonucleotide that binds within a targeted portion of a SHANK3 pre-mRNA, whereby the level of SHANK3 mRNA encoding full length, functional SHANK3 is increased, wherein the sequence of the targeted portion corresponds to **SEQ ID NO:1** or **SEQ ID NO:18751**.

In a related aspect provided herein is a vector for expression, in a mammalian neuron, of an antisense RNA (AR) that binds within a targeted portion of a SHANK3, whereby the level of SHANK3 mRNA encoding full length, functional SHANK3 is increased, wherein the sequence of the targeted portion corresponds to **SEQ ID NO:1**. In some examples the vector includes a neuron-selective promoter for driving expression of the antisense RNA in the mammalian neuron. In some examples the neuron-selective promoter is selective for expression in a neuron type selected from the list consisting of: cortical excitatory neurons, cortical inhibitory neurons, hippocampal excitatory neurons, hippocampal inhibitory neurons, striatal inhibitory neurons, striatal excitatory neurons, cerebellar excitatory neurons, cerebellar inhibitory neurons, and GABAergic neurons. In some examples the vector includes an inducible promoter. In some examples the vector is a non-viral vector. In some examples a non-viral vector further comprises a

transfection agent. In other examples the vector is a viral vector. In some examples, where the vector is a viral vector, the viral vector is a recombinant virus selected from the group consisting of: adeno-associated virus (AAV), adenovirus, lentivirus, and anellovirus.

5 In some examples of any of the foregoing ASOs or vectors, binding of the antisense oligonucleotide or AR to the SHANK3 pre-mRNA modulates splicing of a SHANK3 mRNA derived therefrom. In some examples of any of the foregoing methods, ASOs, vectors, or compositions, the modulation of splicing reduces a level of aberrant retention of an intron. In some examples the sequence of an antisense oligonucleotide or
10 AR disclosed herein includes up to two base mismatches to the targeted portion.

In some examples the nucleotide sequence of the ASO or AR is at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% complementary to the nucleotide sequence of the targeted portion over the length of the ASO or the AR. In some examples the nucleotide sequence of the ASO or AR that binds to a targeted portion of the SHANK3
15 pre-mRNA corresponds to any one of **SEQ ID NOs:4584-16253**.

In some examples any of the foregoing ASOs include a backbone modification. In some examples the backbone modification includes a phosphorothioate linkage or a phosphorodiamidate linkage. In other examples the ASO includes a phosphorodiamidate morpholino, an arabinonucleic acid, a locked nucleic acid, a peptide nucleic acid, or a 2'-
20 O- modification such as a 2'-O-methyl, a 2'-Fluoro, or a 2'-O-methoxyethyl moiety. In some examples the ASO includes at least one modified sugar moiety. In other examples each sugar moiety in the ASO is a modified sugar moiety. In some examples the ASO includes a 2'-O-methoxyethyl moiety. In other examples each nucleotide of the ASO includes a 2'-O-methoxyethyl moiety.

25 In some examples of any of the foregoing ASOs or vectors, the nucleotide sequence of the ASO or AR is 10 to 50 nucleotides, 15 to 40 nucleotides, 18 to 40 nucleotides, 17 to 25 nucleotides, 20 to 35 nucleotides, 20 to 30 nucleotides, 22 to 30 nucleotides, 24 to 30 nucleotides, 25 to 30 nucleotides, or 26 to 30 nucleotides in length. In some examples. In some examples of any of the foregoing ASOs or vectors, the
30 nucleotide sequence of the ASO or AR is 17 to 30 nucleotides in length.

In some examples any of the foregoing ASOs also includes a linked functional moiety. In some examples the functional moiety includes a delivery moiety. In some examples the delivery moiety is selected from the group consisting of: lipids, peptides, carbohydrates, and antibodies. In some examples, wherein the ASO includes a delivery moiety, the delivery moiety includes a cell-penetrating peptide (CPP). In some examples the delivery moiety includes a N-acetylgalactosamine (GalNAc) or glycan moiety. In some examples the delivery moiety includes a fatty acid or lipid moiety. In some embodiments the fatty acid chain length is about C8 to C20. In other examples the functional moiety includes a stabilising moiety. In some examples the functional moiety is covalently linked to the ASO. In other examples the functional moiety is non-covalently linked to the ASO. In some examples the functional moiety is linked to the 5' end of the ASO. In other examples the functional moiety is linked to the 3' end of the ASO. In some embodiments of any of the foregoing methods, the level of SHANK3 protein in at least a plurality of mammalian cells is increased about 1.1 to about 5 fold in cells (e.g., neurons) in vitro or ex vivo, e.g., 1.2 fold, 1.3 fold, 1.5 fold, 1.7 fold, 2 fold, 2.2 fold, 2.5 fold, 2.7 fold, 3 fold, 3.3 fold, 3.5 fold, 4 fold, 4.3 fold, 4.5 fold, 4.7 fold, or another increase in SHANK3 protein levels from about 1.1 fold to about 5 fold in cells in a subject or in vitro or in vivo, compared to the level in a plurality of mammalian cells in the absence of the oligonucleotide or the antisense RNA.

In a related aspect provided herein is a pharmaceutical composition that includes any of the foregoing ASOs or vectors and a pharmaceutically acceptable excipient.

In a further related aspect provided herein is a method for preventing or treating a condition associated with SHANK3 haploinsufficiency, the method comprising administering to a subject in need thereof a therapeutically effective amount of the foregoing pharmaceutical composition. In some examples the condition to be treated is Phelan-McDermid syndrome, an autism spectrum disorder, schizophrenia, or an intellectual disability. In some examples the condition to be treated is Phelan-McDermid syndrome. In some examples the subject to be treated is a human subject.

In a further aspect provided herein is the use of any of the foregoing antisense oligonucleotides, vectors, or compositions in the manufacture of a medicament for prevention or treatment of a condition associated with SHANK3 haploinsufficiency.

In some examples of the foregoing methods of treatment or uses, the level of SHANK3 protein in a least a plurality of cells in the subject is increased about 1.1 to about 5 fold in cells (e.g., neurons) in vitro or ex vivo, e.g., 1.2 fold, 1.3 fold, 1.5 fold, 1.7 fold, 2 fold, 2.2 fold, 2.5 fold, 2.7 fold, 3 fold, 3.3 fold, 3.5 fold, 4 fold, 4.3 fold, 4.5 fold, 4.7 fold, or another increase in SHANK3 protein levels from about 1.1 fold to about 5 fold in cells in a subject or in vitro or in vivo. compared to the level in the absence of the pharmaceutical composition.

In yet another aspect provided herein is a genetically modified cell comprising any of the foregoing ASOs or vectors. In some examples the genetically modified cell is a mammalian cell. In some examples the genetically modified mammalian cell is a human cell. In some examples the genetically modified mammalian cell is a neuron or a neural progenitor. In some examples, the genetically modified mammalian cell is a neuron selected from the group consisting of: cortical glutamatergic neurons, cortical GABAergic neurons, hippocampal glutamatergic neurons, and striatal inhibitory neurons. In some examples the genetically modified mammalian cell is from a cell line. In some examples the cell line is a hiPSC cell line or a cell line derived from neurons.

Brief Description of the Accompanying Drawings

Figure 1 – Illustration of *SHANK3* transcript and ASO target region. (A) SHANK3 transcript model (gene id ENSG00000251322.11 from Gencode v45). Exons and introns are indicated in black color and 5' and 3' UTRs indicated in lighter color. ASOs were designed to target the 3' UTRs of *SHANK3* transcript to mediate upregulation of SHANK3 gene expression. (B) seed sequence of hsa-mir-504-5p, a target sequence for the miRNA hsa-mir-504-5p. (C) Negative SHANK3 gene expression regulation partly induced by the binding of hsa-mir-504-5p to the 3' UTR of SHANK3 mRNA at its target site sequence, resulting in a reduction of SHANK3 protein. (D) illustration of a model in which a steric-blocking ASO binds directly to the 3' UTR of SHANK3 transcripts inhibiting the binding of hsa-mir-504-5p and its induction of RNA degradation leading to a net increase in *SHANK3* transcript levels and SHANK3 protein production.

Figure 2 – Human whole brain *SHANK3* mRNA and hsa-mir-504-5p expression during human neurodevelopment. *SHANK3* mRNA expression was measured using poly-A enriched bulk single-ended RNA-seq data from samples across all brain regions at 9 prenatal and 18 postnatal time points. (PCW, post-conception week; M, months; Y, years; cpm, counts per million)

Figure 3 – PPMO screen in SH-SY5Y cells to upregulate SHANK3 protein expression. SHANK3 protein expression was assessed in PPMO treated SH-SY5Y cells using an ELISA assay. A non-targeting control (NTC), predicted not to hybridize to human transcripts, was included as a negative control. Bar graph represents mean $\pm$ S.D. n=2 independent experiments with 3 technical replicates per experiment. UT = untreated cells. NTC = non-targeting control. PPMOs with **SEQ ID NOs: 160 and 687** were selected for further evaluation in iPSC-derived neurons.

Figure 4 – PPMO effect on SHANK3 protein expression in iPSC-derived glutamatergic neurons. iPSC-derived glutamatergic neurons derived from healthy controls (non-PMS controls) were incubated with a peptide-conjugated PMO (**SEQ ID NOs: 160 and 687**) in triplicate and a non-targeting control (NTC) for 7 days. A non-targeting control, predicted not to hybridize to human transcripts, was included as a negative control. Bar graph represents mean $\pm$ S.D. of SHANK3 protein normalized to total protein amount loaded relative that of untreated cells. n=1 biological replicate per cell line. UT = untreated cells. NTC = non-targeting control.

Figure 5 – SHANK3 protein analysis in PPMO-treated iPSC-glutamatergic neurons derived from Phelan-McDermid Syndrome (PMS). iPSCs derived from in a PMS patient harboring a heterozygous large deletion in the *SHANK3* gene, were differentiated into glutamatergic neurons used to test the efficacy of a PPMO targeted to the *SHANK3* transcript. The PPMO has an oligonucleotide sequence corresponding to “SEQ ID NO: 1847” (originally disclosed in WO 2023/235915) linked to a CPP (**SEQ ID NO:2** originally disclosed as “SEQ ID NO:12694” in WO 2023/235915) and was incubated with iPSC-derived glutamatergic neurons in triplicate for 7 days. A non-targeting control,

predicted not to hybridize to human transcripts, was included as a negative control. Bar graph represents mean $\pm$ S.D. of SHANK3 protein normalized to total protein amount loaded relative that of untreated cells. n=1 biological replicate. UT = untreated cells. Graph was generated using GraphPad Prism Ver 10.2.3 software. *p<0.05, **p<0.005, ***p<0.001. One-Way ANOVA.

Figure 6 – SHANK3 protein isoform analysis in ASO-treated hiPSC (non-affected subject)-derived glutamatergic neurons. iPSC-derived glutamatergic neurons were incubated with an ASO (SEQ ID NO: 1193 disclosed in WO 2023/235915) in triplicate for 7 days. Bar graph represents mean $\pm$ S.D. of the SHANK3 protein isoform, normalized to the respective SHANK3 isoform relative to that of untreated cells. n=1 biological replicate per cell line. UT = untreated cells. Levels of each of the major isoforms evaluated were increased, and the relative ratio of expression levels between the essential isoforms appears unchanged.

Figure 7 – Illustration of SHANK3 transcript and ASO design within the target region of the 3' UTR of SHANK3 transcript. (A) *SHANK3* transcript model (gene id ENSG00000251322.11 from Gencode v45) is depicted, with exons and introns shown in dark gray and the 5' and 3' UTRs in a lighter shade. (B) A segment of the 3' UTR sequence corresponding to **SEQ ID NO:1079**. The miR-504 seed sequence is highlighted in bold. (C) A black line indicates the target sequences of ASOs, designed to upregulate SHANK3 gene expression. This is achieved by altering the secondary structure of mRNA or steric blocking the binding of regulators that reduce the efficacy of SHANK3 protein translation. The numbers correspond to SEQ ID numbers of ASOs as disclosed herein (see also Tables 1-3 of the Appendix); locked nucleic acid (LNA)-modified sequences are marked with a (*) after their SEQ ID number.

Figure 8 – Effect of 2'MOE on SHANK3 protein levels in human iPSC-derived glutamatergic neurons. The bar plots represent the mean $\pm$ SD of SHANK3 protein normalized to the total protein amount loaded, relative to the normalized SHANK3 protein of untreated cells (y-axis). Data is derived from three technical replicates from one biological replicate. Bar plots in white represent untreated cell controls (UT) and to

non-targeting control (NTC) at 1 μ M; grey bars represent ASO-treated cells at 0.5 μ M; and black bars represent ASO-treated cells at 1 μ M. ASOs are split by length. The dotted line represents the baseline of untreated cells at 1. UT refers to untreated cells and NTC indicates the non-targeting control. Graph was generated using GraphPad Prism Version 10.2.3 software.

Figure 9 – Effect of selected MOEs on SHANK3 protein levels in human iPSC- derived neurons. The bar plots represent the mean $\pm$ SD of SHANK3 protein normalized to the total protein amount loaded, relative to the normalized SHANK3 protein of untreated cells (y-axis). Data is derived from three technical replicates from one biological replicate. Bar plots in colour white correspond to untreated cell controls (UT) and to non-targeting control (NTC) at highest concentration (30 μ M); striped pattern to cells treated with a 7.5 μ M dose; grey colour to cells treated with a 15 μ M dose; and black colour to cells treated with a 30 μ M dose. The bar graphs are grouped by ASO length used in the corresponding experiments. The dotted line represent the baseline of untreated cells at 1.0-fold change. UT stands for untreated cells and NTC for non-targeting control. Graph was generated using GraphPad Prism Version 10.2.3 software.

Figure 10 – Effect of selected LNA modified 2'MOE on SHANK3 protein levels in human iPSC- derived neurons. The bar plots represent the mean $\pm$ SD of SHANK3 protein normalized to the total protein amount loaded, relative to the normalized SHANK3 protein of untreated cells (y-axis). Data is derived from three technical replicates from one biological replicate. Bar plots in colour white correspond to untreated cell controls (UT) and to non-targeting control (NTC) at highest concentration (30 μ M); striped pattern to cells treated with a 7.5 μ M dose; grey colour to cells treated with a 15 μ M dose; and black colour to cells treated with 30 μ M dose. The dotted line represents the baseline of untreated cells at 1.0-fold change. Panel (A) shows the SHANK3 protein changes after the treatment with 18-mer ASOs with sequences corresponding to **SEQ ID NOs: 1091, 1093, and 1092**; while panel (B) shows the ASO derivatives from a 15-mer, a 17-mer and a 20-mer with sequences corresponding to **SEQ ID NOs: 1084, 1094, and**

1087, respectively. UT stands for untreated cells and NTC for non-targeting control. Graphs were generated using GraphPad Prism Version 10.2.3 software.

Figure 11 – Effect of selected MOEs on SHANK3 protein levels in human iPSC- derived neurons from Phelan-McDermid Syndrome patients. The bar plots represent the mean $\pm$ SD of SHANK3 protein normalized to the total protein amount loaded, relative to the normalized SHANK3 protein of untreated cells (y-axis). Data is derived from three technical replicates from one biological replicate. Panel (A) shows changes in SHANK3 protein levels following treatment with ASOs corresponding to **SEQ ID NOs: 1094, 1087, 1091, 1093, and 1092**; in which the white bar indicates untreated controls (UT); bars with stripes represent cells treated at 7.5 μ M; bars with a dotted pattern indicate cells treated at 15 μ M; and bars in solid gray represent cells treated at 30 μ M; and black represent cells treated at 45 μ M. Panel (B) shows changes in SHANK3 protein levels after treatment with **SEQ ID NOs: 1122, 1093, 1091, 1126, 1128, and 1092**. White bar represent untreated controls (UT), striped bar for 7.5 μ M, gray bar for 15 μ M dose, and black bar for 30 μ M. In both panels, dotted lines represent the baseline of untreated cells at 1.0-fold change. UT denotes untreated cells. Graphs were generated using GraphPad Prism Version 10.2.3 software. * p. adj. <0.05, ** p. adj. <0.01, *** p. adj. <0.005, **** p. adj. < 0.001. One-Way ANOVA.

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Figure 12 – Functional assessment of gymnotic ASO treatment in Phelan-McDermid patient iPSC-derived glutamatergic neurons. The bar plots represent the mean $\pm$ SD of the signal intensity of spontaneous calcium oscillations (y-axis). Data is derived from three technical replicates from one biological replicate. Panel (A) shows the baseline signal intensity of spontaneous calcium oscillations in two untreated non-PMS cell lines (SHANK3-non-deficient) shown in white and grey, two untreated PMS patient cell lines (SHANK3-deficient) shown in black. The left side (including PMS patient #1) of the plot corresponds to a 20,000 – 30,000 cells seeding; while the right side (including PMS patient #2) to a 10,000 cells seeding. The dotted line represents the baseline level of spontaneous calcium oscillations signal in untreated SHANK3-non-deficient commercial cells at 1.0-fold change. Panel (B) shows the functional assessment in PMS patient cells

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21 days after a single-dose ASO treatment. White bars represent untreated cell control (UT) and non-targeting control (NTC); grey bars represent cells treated with a 15 μ M ASO; black bar represent cells treated with a 30 μ M concentration. The dotted line represents the untreated baseline at 1.0-fold change. Panel (C) shows the functional assessment in PMS patient cells 21 days after a double-dose ASO treatment, White bar represent control group including untreated cell control (UT), non-targeting control (NTC), negative assay control (BAPTA) and positive assay control (Ionomycin). Black bar represent cells treated with ASO at 15 μ M. The dotted line represents the baseline of untreated cells at 1.0-fold change. UT stands for untreated cells and NTC to non-targeting control. BAPTA is used as an assay control to chelate free calcium ions, thereby suppressing calcium-dependent signaling. Ionomycin acts as a calcium ionophore, increasing intracellular calcium levels by facilitating calcium entry into cells. Graphs were generated using GraphPad Prism Version 10.2.3 software.

15 Detailed Description

General

Throughout this specification, unless specifically stated otherwise or the context requires otherwise, reference to a single step, composition of matter, group of steps or group of compositions of matter shall be taken to encompass one and a plurality (*i.e.*, one or more) of those steps, compositions of matter, groups of steps or groups of compositions of matter. Thus, as used herein, the singular forms “a”, “an” and “the” include plural aspects unless the context clearly dictates otherwise. For example, reference to “a” includes a single as well as two or more; reference to “an” includes a single as well as two or more; reference to “the” includes a single as well as two or more and so forth.

Each example of the present disclosure described herein is to be applied *mutatis mutandis* to each and every other example unless specifically stated otherwise.

Those skilled in the art will appreciate that the disclosure herein is susceptible to variations and modifications other than those specifically described. It is to be understood that the disclosure includes all such variations and modifications. The disclosure also includes all of the steps, features, compositions and compounds referred

to or indicated in this specification, individually or collectively, and any and all combinations or any two or more of said steps or features.

The present disclosure is not to be limited in scope by the specific examples described herein, which are intended for the purpose of exemplification only.

- 5 Functionally-equivalent products, compositions and methods are clearly within the scope of the disclosure, as described herein.

The present disclosure is performed without undue experimentation using, unless otherwise indicated, conventional techniques of molecular biology, microbiology, virology, recombinant DNA technology, peptide synthesis in solution, solid phase
10 peptide synthesis, and immunology. Such techniques are described and explained throughout the literature in sources such as Perbal 1984, Sambrook et al., 2001, Brown (editor) 1991, Glover and Hames (editors) 1995 and 1996, Ausubel *et al.* including all updates until present, Coligan *et al.* (editors) (including all updates until present), Maniatis *et al.* 1982, Gait (editor) 1984, Hames and Higgins (editors) 1984, Freshney
15 (editor) 1986.

The term “and/or”, *e.g.*, “X and/or Y” shall be understood to mean either “X and Y” or “X or Y” and shall be taken to provide explicit support for both meanings or for either meaning.

The term “about”, unless stated to the contrary, refers to $\pm 20\%$, more preferably
20 $\pm 10\%$, of the designated value. For the avoidance of doubt, the term “about” followed by a designated value is to be interpreted as also encompassing the exact designated value itself (for example, “about 10” also encompasses 10 exactly).

Throughout this specification the word “comprise”, or variations such as “comprises” or “comprising”, will be understood to imply the inclusion of a stated
25 element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

The term “antisense oligonucleotide”, “antisense oligomer” or “ASO,” as used herein, encompasses oligonucleotides and any other oligomeric molecule that comprises nucleobases capable of hybridizing to a complementary sequence on a target RNA
30 transcript, including, but not limited to, those that do not comprise a sugar moiety, such

as in the case of a peptide nucleic acid (PNA). Preferably, the ASO is an ASO that is resistant to nuclease cleavage or degradation.

The phrase “binds to a targeted portion” or “binds within a targeted portion,” in reference to an ASO or AR, as used herein, refers to specific hybridization between the ASO or AR nucleotide sequence and a target nucleotide sequence that is complementary within the ranges set forth herein. In some examples the targeted portion comprises the sequence according to **SEQ ID NO:1079**. In some examples the targeted portion consists of the sequence according to **SEQ ID NO:1079**. In some examples, specific hybridization occurs where, under *ex vivo* conditions, the hybridization occurs under high stringency conditions. By “high stringency conditions” is meant that the ASO or AR, under such *ex vivo* conditions, hybridize to a target sequence in an amount that is detectably stronger than non-specific hybridization. High stringency conditions, then, are conditions that distinguish a polynucleotide with an exact complementary sequence, or one containing only a few scattered mismatches from a random sequence that happened to have a few small regions (*e.g.*, 1-5 bases) that matched the probe. Such small regions of complementarity are more easily melted than a full-length complement of 12-17 or more bases, and moderate stringency hybridization makes them easily distinguishable. In one example, high stringency conditions include, for example, low salt and/or high temperature conditions, such as provided by about 0.02-0.1 M NaCl or the equivalent, at temperatures of about 50-70 °C. The skilled person will appreciate that under *in vivo* conditions, the specificity of hybridization between an ASO or an AR and its target sequence is defined in terms of the level of complementarity between the ASO or an AR and the target sequence to which it hybridizes within a cell.

The phrase “antisense oligonucleotide or AR comprises a mismatch to the targeted region” as used herein refers to the fact that the antisense oligonucleotide or AR sequence differs from the reverse complement of the target sequence with which it is to hybridize at the referred-to (mismatched) position. For example, for a target sequence: 5'-AGUGGAUUGCUAGU-3', a perfectly complementary ASO sequence would include 5'-ACUAGCAAUCCACU-3', where the ASO 5'-ACUAGCACUCCACU-3' includes a “base mismatch” with respect to the target sequence at the underlined/bold position.

The term “gymnotic” in reference to an ASO or ASO delivery as used herein refers to delivery of an ASO into cells in the absence of a transfection agent.

The term “peptide” is intended to include compounds composed of amino acid residues linked by amide bonds. A peptide may be natural or unnatural, ribosome translated or synthetically derived. Typically, a peptide will consist of between 2 and 200 amino acids. For example, the peptide may have a length in the range of 10 to 20 amino acids or 10 to 30 amino acids or 10 to 40 amino acids or 10 to 50 amino acids or 10 to 60 amino acids or 10 to 70 amino acids or 10 to 80 amino acids or 10 to 90 amino acids or 10 to 100 amino acids, including any length within said range(s). The peptide may comprise or consist of fewer than about 150 amino acids or fewer than about 125 amino acids or fewer than about 100 amino acids or fewer than about 90 amino acids or fewer than about 80 amino acids or fewer than about 70 amino acids or fewer than about 60 amino acids or fewer than about 50 amino acids.

Peptides, as referred to herein, include “inverso” peptides in which all L-amino acids are substituted with the corresponding D-amino acids, “retro-inverso” peptides in which the sequence of amino acids is reversed and all L-amino acids are replaced with D-amino acids.

Peptides may comprise amino acids in both L- and/or D-form. For example, both L- and D-forms may be used for different amino acids within the same peptide sequence. In some examples the amino acids within the peptide sequence are in L-form, such as natural amino acids. In some examples the amino acids within the peptide sequence are a combination of L- and D-form. Further, peptides may comprise unusual, but naturally occurring, amino acids including, but not limited to, hydroxyproline (Hyp), beta-alanine, citrulline (Cit), ornithine (Orn), norleucine (Nle), 3-nitrotyrosine, nitroarginine, pyroglutamic acid (Pyr). Peptides may also incorporate unnatural amino acids including, but not limited to, homo amino acids, N-methyl amino acids, alpha-methyl amino acids, beta (homo) amino acids, gamma amino acids, and N-substituted glycines. Peptides may be linear peptides or cyclic peptides.

The term “protein” shall be taken to include a single polypeptide chain, *i.e.*, a series of contiguous amino acids linked by peptide bonds or a series of polypeptide chains covalently or non-covalently linked to one another (*i.e.*, a polypeptide complex). For

example, the series of polypeptide chains can be covalently linked using a suitable chemical bond or a disulfide bond. Examples of non-covalent bonds include hydrogen bonds, ionic bonds, Van der Waals forces, and hydrophobic interactions.

Percentage amino acid sequence identity with respect to a given amino acid
5 sequence is defined as the percentage of amino acid residues in a candidate sequence that are identical to the amino acid residues in the reference sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Amino acid sequence identity may be determined using the EMBOSS Pairwise
10 Alignment Algorithms tool available from The European Bioinformatics Institute (EMBL-EBI), which is part of the European Molecular Biology Laboratory. This tool is accessible at the website located at www.ebi.ac.uk/Tools/emboss/align/. This tool utilizes the Needleman-Wunsch global alignment algorithm (Needleman and Wunsch, 1970). Default settings are utilized, which include Gap Open: 10.0 and Gap Extend 0.5.
15 The default matrix "Blosom62" is utilized for amino acid sequences and the default matrix. Percent (%) or percentage "nucleic acid sequence identity" with respect to the nucleotide sequences disclosed herein is defined as the percentage of nucleotides in a candidate sequence that are identical with the nucleotides in the reference sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum
20 percent sequence identity. Alignment for purposes of determining percent nucleic acid sequence identity can be achieved in various ways that are known in the art, for instance, using publicly available computer software such as BLAST or ALIGN. The skilled person can readily determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the
25 sequences being compared.

The term "cell penetrating peptide" (CPP) refers to a peptide that is capable of crossing a cellular membrane. In one example, a CPP is capable of translocating across a mammalian cell membrane and entering into a cell. In another example, a CPP may direct a conjugate to a desired subcellular compartment. Thus, a CPP may direct or
30 facilitate penetration of a molecule of interest across a phospholipid, mitochondrial, endosomal, lysosomal, vesicular, or nuclear membrane. A CPP may be translocated

across the membrane with its amino acid sequence complete and intact, or alternatively partially degraded.

A CPP may direct a molecule of interest, such as an ASO disclosed herein, from outside a cell through the plasma membrane, and into the cytoplasm or a desired subcellular compartment. Alternatively, or in addition, a CPP may direct a molecule of interest across the blood-brain, trans-mucosal, hematoretinal, skin, gastrointestinal and/or pulmonary barriers.

The term “peptide ligand” or “receptor binding peptide” refers to a peptide that is capable of binding to a membrane surface receptor to enable transport of the peptide across a cellular membrane. In one example a peptide ligand may enable transport across the cellular membrane via the natural endocytosis of the targeted receptor. In another example the peptide ligand may utilise a complementary mechanism of transport across the cellular membrane including utilising a conjugated CPP. In one example, a peptide ligand is capable of translocating across a mammalian cell membrane and to enter a cell. In another example, a peptide ligand may direct a conjugate to a desired subcellular compartment. Thus, a peptide ligand may direct or facilitate cellular uptake of a molecule of interest across a phospholipid, mitochondrial, endosomal, lysosomal, vesicular, or nuclear membrane. A peptide ligand may be translocated across the membrane with its amino acid sequence complete and intact, or alternatively partially degraded.

A peptide ligand via its binding to a target receptor may direct a molecule of interest, such as an ASO disclosed herein, from outside a cell through the plasma membrane, and into the cytoplasm or a desired subcellular compartment. Alternatively, or in addition, a peptide ligand via its binding to a target receptor may direct a molecule of interest across a relevant biological barrier, *e.g.*, the blood-brain, trans-mucosal, hematoretinal, skin, gastrointestinal, and/or pulmonary barriers.

Compositions for Increasing SHANK3 Protein Levels

In the case of rare, monogenic diseases, the loss of one functional allele, *e.g.*, *SHANK3* allele, can result in haploinsufficiency and the associated disease.

While not wishing to be bound by theory, it is believed that ASOs can act by a number of mechanisms, including, but not limited to targeting sequences within the 3' UTR of *SHANK3* mRNA that can stabilize *SHANK3* transcripts and/or net translation, *e.g.*, by masking binding sites for miRNAs (*e.g.*, a binding site for miR-504) located within the *SHANK3* mRNA 3' UTR to sterically hinder ("mask") access of these miRNAs to their binding sites, thereby resulting in an increased level of *SHANK3* mRNA and ultimately allowing increased translation of SHANK3 protein. Alternatively, alterations in the secondary structure of the 3' UTR induced by ASO hybridization could also result in increased translation and/or stabilization of the targeted *SHANK3* transcript.

Accordingly, disclosed herein is an ASO that binds within a targeted portion of the 3' UTR of a SHANK3 mRNA; whereby binding of the antisense oligonucleotide within the targeted portion in a mammalian cell results in an increased level of SHANK3 protein in the mammalian cell.

For reference, the nucleotide sequence of the canonical human *SHANK3* mRNA 3' UTR is provided herein as **SEQ ID NO:1** (provided in the Appendix). In some examples the targeted portion comprises the sequence according to **SEQ ID NO:1079**. In some examples the targeted portion consists of the sequence according to **SEQ ID NO:1079** (provided in the Appendix).

Antisense Oligonucleotides (ASOs) and Antisense RNAs (ARs)

In some examples of the compositions and methods described herein, ASOs and ARs have a sequence that is completely or nearly completely complementary across its length to the target sequence. ASOs and ARs are designed so that they bind (hybridize) to a target RNA sequence (*e.g.*, a targeted portion of a mRNA transcript) and remain hybridized under physiological conditions. Selection of suitable sequences for ASOs and ARs generally avoids, where possible, similar nucleic acid sequences in other (*i.e.*, off-target) locations in the genome or in cellular mRNAs or miRNAs, such that the likelihood the ASO or AR will hybridize at such sites is limited. In some examples, ASOs disclosed herein bind to a targeted region within the *SHANK3* mRNA 3' UTR.

In some examples, ASOs or ARs "specifically hybridize" to or are "specific" to a target nucleic acid or a targeted portion of a *SHANK3* mRNA 3' UTR. At a given ionic

strength and pH, the T_m is the temperature at which 50% of a target sequence hybridizes to a complementary oligonucleotide.

ASO and AR sequences are “complementary” to their target sequences when hybridization occurs in an antiparallel configuration between two single-stranded polynucleotides. Complementarity is quantifiable in terms of the proportion (*e.g.*, the percentage) of bases in opposing strands that are expected to form hydrogen bonds with each other, according to generally accepted base-pairing rules. The nucleotide sequence of an ASO or AR need not be 100% complementary to that of its target nucleic acid to hybridize. In certain examples, the nucleotide sequences of ASOs or ARs in the compositions disclosed herein can be at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence complementary to the nucleotide sequence of the targeted portion of an RNA transcript over the length of the ASO or AR nucleotide sequence. For example, an ASO or AR in which 18 of 20 nucleotides of ASO or AR sequence are complementary to a target region, and would therefore specifically hybridize, would represent 90 percent complementarity. In such an example, the remaining non-complementary nucleotides of the ASO or AR could be clustered together or interspersed with complementary nucleotides and need not be contiguous. Complementarity of an ASO or AR sequence to a target nucleotide sequence (expressed as “percent complementarity” to its target sequence; or “percent identity” to its reverse complement sequence) can be determined routinely using algorithms known in the art, as exemplified in the BLAST programs (basic local alignment search tools) and PowerBLAST programs (Altschul, et al., 1990, *J. Mol. Biol.*, 215:403-410; Zhang et al., 1997, *Genome Res.*, 7:649-656).

In some examples, an ASO or AR does not hybridize to all nucleotides in a target sequence and the nucleotide positions at which it does hybridize may be contiguous or noncontiguous. ASOs or ARs may hybridize over one or more segments of a *SHANK3* mRNA 3' UTR such that intervening or adjacent segments (*e.g.*, one or more abasic spacer subunits) are not involved in the hybridization event (*e.g.*, a loop structure or hairpin structure may be formed).

In some examples the nucleotide sequence of the ASO or the AR is at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% complementary to the nucleotide sequence of the targeted portion of the *SHANK3* mRNA over the length of the ASO or the AR. In some examples the nucleotide sequence of the ASO or the AR comprises a sequence that: (a) has at least about 40% identity to about 60% identity of the nucleotide sequence of an ASO or AR sequence disclosed herein, *e.g.*, 45% identity, 48% identity, 50% identity, 52% identity, 55% identity, 58% identity or another sequence identity from about 40% identity to about 60% identity to the entire length of the sequence of any ASO or AR disclosed herein; and (b) comprises a contiguous sequence of at least 8 bases to 16 bases that is 100% identical to a contiguous sequence of at least 8 to 16 bases in any one of the ASO or AR sequences disclosed herein, *e.g.*, 100% sequence-identical to a contiguous 9 bases, 10 bases, 11 bases, 12 bases, 13 bases, 14 bases, 15 bases, or 16 bases of an ASO or AR sequence disclosed herein. The ASOs or ARs for use in the compositions described herein may be of any length suitable for specific hybridization to a target sequence. In some examples, the nucleotide sequence of the ASOs or ARs consist of 8 to 50 nucleotides. For example, the ASO or AR sequence can be 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 40, 45, or 50 nucleotides in length. In some examples, the nucleotide sequence of the ASOs or ARs consist of 8 to 50 nucleotides. For example, the ASO or AR sequence can be 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 40, 45, or 50 nucleotides in length. In some examples, the ASOs consist of more than 50 nucleotides, but no more than 100 nucleotides in length. In some examples, the ASO or AR nucleotide sequence is from 8 to 50 nucleotides, 8 to 40 nucleotides, 8 to 35 nucleotides, 8 to 30 nucleotides, 8 to 25 nucleotides, 8 to 20 nucleotides, 8 to 15 nucleotides, 9 to 50 nucleotides, 9 to 40 nucleotides, 9 to 35 nucleotides, 9 to 30 nucleotides, 9 to 25 nucleotides, 9 to 20 nucleotides, 9 to 15 nucleotides, 10 to 50 nucleotides, 10 to 40 nucleotides, 10 to 35 nucleotides, 10 to 30 nucleotides, 10 to 25 nucleotides, 10 to 20 nucleotides, 10 to 15 nucleotides, 11 to 50 nucleotides, 11 to 40 nucleotides, 11 to 35 nucleotides, 11 to 30 nucleotides, 11 to 25 nucleotides, 11 to 20 nucleotides, 11 to 15 nucleotides, 12 to 50 nucleotides, 12 to 40 nucleotides, 12 to 35 nucleotides, 12 to 30 nucleotides, 12 to 25 nucleotides, 12 to 20 nucleotides, 12 to 15

nucleotides, 13 to 50 nucleotides, 13 to 40 nucleotides, 13 to 35 nucleotides, 13 to 30 nucleotides, 13 to 25 nucleotides, 13 to 20 nucleotides, 14 to 50 nucleotides, 14 to 40 nucleotides, 14 to 35 nucleotides, 14 to 30 nucleotides, 14 to 25 nucleotides, 14 to 20 nucleotides, 15 to 50 nucleotides, 15 to 40 nucleotides, 15 to 35 nucleotides, 15 to 30 nucleotides, 15 to 25 nucleotides, 15 to 20 nucleotides, 17 to 30 nucleotides, 17 to 25 nucleotides, 17 to 20 nucleotides, 20 to 50 nucleotides, 20 to 40 nucleotides, 20 to 35 nucleotides, 20 to 30 nucleotides, 20 to 25 nucleotides, 25 to 50 nucleotides, 25 to 40 nucleotides, 25 to 35 nucleotides, or 25 to 30 nucleotides in length. In some examples, the ASOs or ARs are 17 nucleotides in length. In other examples, the ASOs or ARs are 20 nucleotides in length. In some examples, the nucleotide sequence of the ASO or AR nucleotide is 25 nucleotides in length.

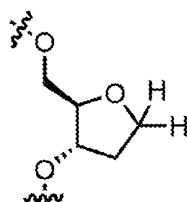
In other examples the ASOs or ARs comprise at least 10 contiguous nucleotides of an ASO or AR sequence described herein. In some examples ASOs or ARs comprise at least 10 contiguous nucleotides (subsequence) from each of two or more ASO or AR sequences described herein, where the two or more subsequences are not contiguous in a *SHANK3* mRNA sequence.

In some examples for each occurrence of “G” in an ASO or AR sequence disclosed herein, the “G” is guanosine or inosine. In some examples for each occurrence of “T” in an ASO or AR sequence disclosed herein, the “T” is any one of: thymidine, inosine, uracil, or an isomeric or modified form of uracil (e.g., pseudouridine or N1-methyl-pseudouridine). In some examples for each occurrence of “C” in an ASO or AR sequence disclosed herein, the C is cytosine or a modified form of cytosine (e.g., 5'-methyl cytosine).

In some examples the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1080-1093** or **1096-1133**. In some examples the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1080-1093**. In some examples the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1084, 1087, or 1091-1093**. In some examples the nucleotide sequence of the ASO corresponds to **SEQ ID NO:1084**. In some examples the nucleotide sequence of the ASO corresponds to **SEQ ID NO:1087**. In some examples the nucleotide sequence of the ASO corresponds to **SEQ ID NO:1091**. In some examples the nucleotide sequence of the ASO

corresponds to **SEQ ID NO:1092**. In some examples the nucleotide sequence of the ASO corresponds to **SEQ ID NO:1093**.

In some examples any of the foregoing ASOs include a backbone modification. In some examples the backbone modification includes a phosphorothioate linkage or a phosphorodiamidate linkage. In other examples the ASO includes a phosphorodiamidate morpholino, an arabinonucleic acid, a locked nucleic acid, a peptide nucleic acid, a 2'-*O*-modification such as a 2'-*O*-methyl, a 2'-Fluoro, or a 2'-*O*-methoxyethyl moiety, or an abasic spacer subunit. In some examples the abasic spacer subunit comprises the structure according to Formula I:



Formula I

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In some examples the nucleotide sequence of the ASO comprises one or more abasic spacer subunit and/or one or more locked nucleic acids (LNAs). In some examples the nucleotide sequence of the ASO comprises one or more abasic spacer subunits and one or more LNAs. In some examples, where the ASO comprises at least one abasic spacer subunit, at least one locked nucleic acid, or both, the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1096-1133**.

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In some examples the ASO includes at least one modified sugar moiety. In other examples each sugar moiety in the ASO is a modified sugar moiety. In some examples the ASO includes a 2'-*O*-methoxyethyl moiety. In other examples each nucleotide of the ASO includes a 2'-*O*-methoxyethyl moiety.

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In some examples the nucleotide sequence of the ASO or AR comprises the sequence of any one of **SEQ ID NOs:3-1078**. In some examples the nucleotide sequence of the ASO or AR comprises the sequence of **SEQ ID NO:160** or **SEQ ID NO:687**. In some examples the nucleotide sequence of the ASO or AR comprises the sequence of **SEQ ID NO:160**. In some examples the nucleotide sequence of the ASO or AR

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comprises the sequence of **SEQ ID NO:687**. In some examples the nucleotide sequence of the ASO comprises the nucleotide sequence of **SEQ ID NO:160**. In other examples the nucleotide sequence of the ASO comprises the nucleotide sequence of **SEQ ID NO:160**.

5 In some examples the nucleotide sequence of the ASO or AR consists of the nucleotide sequence of any one of **SEQ ID NOs:3-1078**. In some examples the nucleotide sequence of the ASO or AR consists of the nucleotide sequence of **SEQ ID NO:160** or **SEQ ID NO:687**. In some examples the nucleotide sequence of the ASO or AR consists of **SEQ ID NO:160**. In some examples the nucleotide sequence of the ASO
10 or AR consists of **SEQ ID NO:687**. In some examples the nucleotide sequence of the ASO consists of **SEQ ID NO:160**. In some examples the nucleotide sequence of the ASO consists of **SEQ ID NO:687**. Sequences for the foregoing **SEQ ID NOs** are provided in Tables 1-3 in the Appendix.

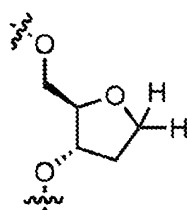
15 *ASO Chemistry and Modifications*

 The ASOs used in the compositions described herein may comprise naturally-occurring nucleotides, nucleotide analogues, modified nucleotides, or any combination thereof. The term “naturally occurring nucleotides” includes deoxyribonucleotides and ribonucleotides. The term “modified nucleotides” includes nucleotides with modified or
20 substituted sugar groups and/or having a modified backbone. In some examples, all the nucleotides of an ASO are modified nucleotides. Chemical modifications of ASOs or components of ASOs that are compatible with the compositions and methods described herein are known in the art as disclosed in, *e.g.*, in U.S. Patent No. 8,258,109, U.S. Patent No. 5,656,612, U.S. Patent Publication No. 2012/0190728, and Roberts et al., 2020,
25 *Nature Rev. Drug Disc.*, 19:673-694.

 One or more nucleotides of an ASO may be any naturally occurring, unmodified nucleobase such as adenine, guanine, cytosine, thymine, uracil and inosine, or any synthetic or modified nucleobase that is sufficiently similar to an unmodified nucleobase such that it is capable of hydrogen bonding with a nucleobase present on a target RNA
30 transcript. Examples of suitable modified nucleobases include, but are not limited to,

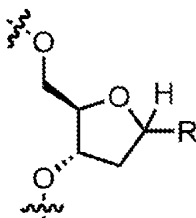
hypoxanthine, xanthine, 7-methylguanine, 5, 6-dihydrouracil, 5-methylcytosine, and 5-hydroxymethoylcytosine.

- 5 In some examples an ASO includes 1, 2, or 3 abasic spacer subunits, residues that comprise a sugar backbone but do not include a nucleobase, interspersed at various positions within an ASO sequence. Abasic “spacer” subunits and their use in oligonucleotides is described in, *e.g.*, PCT/US2022/044995. In some preferred examples the abasic spacer subunit comprises the structure according to Formula I:



Formula I

- 10 In some examples an abasic spacer subunit comprises the structure according to Formula II:



Formula II

In some examples an ASO disclosed herein includes 1-3 abasic spacer subunits and 1-3 locked nucleic acid subunits.

- 15 ASOs include a “backbone” structure, that refers to the connection between nucleotides/monomers of the ASO. In naturally occurring oligonucleotides, the backbone comprises a 3′-5′ phosphodiester linkage connecting sugar moieties of adjacent nucleotides. Suitable types of backbone linkages for the ASOs described herein include, but are not limited to, phosphodiester, phosphorothioate, phosphorodithioate,

phosphorodiamidate, phosphoroselenoate, phosphorodiselenoate, phosphoroanilothioate, phosphoraniladate, phosphoramidate, and the like. In some examples, the backbone modification is a phosphorothioate linkage. In other examples, the backbone modification is a phosphorodiamidate linkage. See, *e.g.*, Roberts et al. 5 *supra*; and Agrawal (2021), *Biomedicines*, 9:503. In some examples, the backbone structure of the ASO does not contain phosphorous-based linkages, but rather contains peptide bonds, for example in a peptide nucleic acid (PNA), or linking groups including carbamate, amides, and linear and cyclic hydrocarbon groups.

In some examples, the stereochemistry at each of the phosphorus internucleotide 10 linkages of the ASO backbone is random. In other examples, the stereochemistry at each of the phosphorus internucleotide linkages of the ASO backbone is controlled and is not random. For example, U.S. Pat. No. 9,605,019 describes methods for independently selecting the handedness of chirality at each phosphorous atom in an oligonucleotide. In some examples, an ASO used in the compositions and methods provided herein, 15 including, but not limited to, the ASOs the sequences of which are disclosed herein as **SEQ ID NOs:1080-1093, 1096-1133, SEQ ID NOs:3-1078** (*e.g.*, **SEQ ID NO:160** or **SEQ ID NO:687**), and **SEQ ID NOs: 1080-1133**. In some examples, a composition or composition used in the methods disclosed herein comprises a pure diastereomeric ASO. In other examples, the composition comprises an ASO that has diastereomeric purity of 20 at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, about 100%, about 90% to about 100%, about 91% to about 100%, about 92% to about 100%, about 93% to about 100%, about 94% to about 100%, about 95% to about 100%, about 96% to about 100%, about 97% to about 100%, about 98% to 25 about 100%, or about 99% to about 100%.

In some examples, the ASO has a non-random mixture of Rp and Sp configurations at its phosphorus internucleotide linkages. In some examples, an ASO used in the compositions and methods disclosed herein, comprises about 5-100% Rp, at least about 5% Rp, at least about 10% Rp, at least about 15% Rp, at least about 20% Rp, 30 at least about 25% Rp, at least about 30% Rp, at least about 35% Rp, at least about 40% Rp, at least about 45% Rp, at least about 50% Rp, at least about 55% Rp, at least about

60% Rp, at least about 65% Rp, at least about 70% Rp, at least about 75% Rp, at least about 80% Rp, at least about 85% Rp, at least about 90% Rp, or at least about 95% Rp, with the remainder Sp, or about 100% Rp.

In some examples, the ASOs described herein contain a sugar moiety that
5 comprises ribose or deoxyribose, or a modified sugar moiety or sugar analogue, including a morpholine ring. Suitable examples of modified sugar moieties include, but are not limited to, 2' substitutions such as 2'-O-modifications, 2'-O-methyl (2'-O-Me), 2'-O-methoxyethyl (2'MOE), 2'-O-aminoethyl, 2'F, N3'→P5' phosphoramidate, 2'dimethylaminoethoxy, 2'dimethylaminoethoxyethoxy, 2'-guanidinidium, 2'-O-guanidinium ethyl, 2'-deoxy-2'-fluoroarabinonucleic acid (2'FANA), carbamate
10 modified sugars, and bicyclic modified sugars. In some examples, the sugar moiety modification is selected from among 2'-O-Me, 2'F, and 2'MOE. In other examples, the sugar moiety modification is an extra bridge bond, such as in a locked nucleic acid (LNA). In some examples the sugar analogue contains a morpholine ring, such as
15 phosphorodiamidate morpholino (PMO). In some examples, the sugar moiety comprises a ribofuransyl or 2'deoxyribofuransyl modification. In some examples, the sugar moiety comprises 2'4'-constrained 2'-O-methoxyethyl (cMOE) modifications. In some examples, the sugar moiety comprises cEt 2', 4' constrained 2'-O ethyl BNA modifications. In other examples, the sugar moiety comprises tricycloDNA (tcDNA)
20 modifications. In some examples, the sugar moiety comprises ethylene nucleic acid (ENA) modifications. In some examples, the sugar moiety comprises 2'-O-(2-N-methylcarbamoyl) (MCE). Modifications are known in the art as exemplified in Jarver, et al., 2014, *Nucleic Acid Therapeutics*, 24(1): 37-47.

In some examples, each constituent nucleotide of the ASO is modified in the same
25 way, e.g., every linkage of the backbone of the ASO comprises a phosphorothioate linkage, or each ribose sugar moiety comprises a 2'-O-methyl modification. In other examples, a combination of different modifications is used, e.g., an ASO comprising a combination of phosphorodiamidate linkages and sugar moieties comprising morpholine rings (morpholinos).

30 In some examples, the ASO comprises one or more backbone modifications. In some examples, the ASO comprises one or more sugar moiety modification. In some

examples, the ASO comprises one or more backbone modifications and one or more sugar moiety modifications. In some examples, the ASO comprises a 2'MOE modification and a phosphorothioate backbone. In some examples, the ASO comprises a peptide nucleic acid (PNA).

- 5 In some preferred examples, the ASO comprises a phosphorodiamidate morpholino (PMO).

The skilled person in the art will appreciate that ASOs may be modified in order to achieve desired properties or activities of the ASO or reduce undesired properties or activities of the ASO. In some examples, an ASO is modified to alter one or more
10 properties. For example, such modifications can: enhance binding affinity to a target sequence on a pre-mRNA transcript; reduce binding to any non-target sequence; reduce degradation by cellular nucleases (*e.g.*, RNase H); improve uptake of an ASO into a cell and/or particular subcellular compartments; alter the pharmacokinetics or pharmacodynamics of the ASO; and/or modulate the half-life of the ASO *in vivo*.

- 15 In some examples, the ASOs comprise one or more 2'-O-(2-methoxyethyl) (MOE) phosphorothioate-modified nucleotides, which have been shown to confer significantly enhanced resistance of ASOs to nuclease degradation and increased bioavailability.

In some examples the ASOs comprise one or more abasic spacer subunits, which
20 may reduce off-target hybridization of the ASO.

Methods for synthesis and chemical modification of ASOs, as well as synthesis of ASO conjugates is well known in the art, and such ASOs are available commercially.

- In some examples, a composition (*e.g.*, a pharmaceutical composition) provided here includes two or more ASOs with different chemistries but complementary to the
25 same targeted portion of the *SHANK3* mRNA 3' UTR. In other examples, a composition comprises two or more ASOs that are complementary to different targeted portions of the 3' UTR.

In some examples, the compositions disclosed herein include ASOs that are linked to a functional moiety. In some examples, the functional moiety is a delivery moiety, a
30 targeting moiety, a detection moiety, a stabilizing moiety, or a therapeutic moiety. In some examples the functional moiety includes a delivery moiety or a targeting moiety.

In some examples the functional moiety includes a stabilizing moiety. In some preferred examples the functional moiety is a delivery moiety.

Suitable delivery moieties include, but are not limited to, lipids, polyethers, peptides, carbohydrates, glycans, receptor binding peptide (RBP), and antibodies.

5 In some examples, the delivery moiety includes a cell-penetrating peptide (CPP). Suitable examples of CPPs are described in, *e.g.*, PCT/AU2020/051397. In some examples the amino acid sequence of the CPP comprises or consists of: RRSRTARAGRPRN SSRPSAPR (SEQ ID NO:2). In other examples, the delivery moiety includes a RBP.

10 In other examples, the delivery moiety includes a carbohydrate. In some examples, a carbohydrate delivery moiety is selected from among N-acetylgalactosamine (GalNAc), N-Ac-Glucosamine (GluNAc), glycan, and a mannose. In one example, the carbohydrate delivery moiety comprises GalNAc or a glycan moiety.

In other examples, the delivery moiety includes a lipid. In some examples the lipid
15 contains saturated acids. In some examples the lipid contains unsaturated acids. In some examples the lipid contains saturated and unsaturated acids. Examples of suitable lipids as delivery moieties include, but are not limited to, cholesterol moiety, a cholesteryl moiety, and aliphatic lipids. In some examples the delivery moiety includes a fatty acid or lipid moiety. In some embodiments the fatty acid chain length is about C8 to C20.
20 Examples of suitable fatty acid moieties and their conjugation to oligonucleotides are found in, *e.g.*, International Patent Publication WO 2019232255 and in Prakash et al., (2019).

In further examples, the delivery moiety includes an antibody, as described in, *e.g.*, Dugal-Tessier et al., (2021).

25 Suitable examples of stabilizing moieties include, but are not limited to, polyethylene glycol (PEG), poly(oligo(ethylene glycol) methyl ether methacrylate) (POEGMA), and Poly(2-oxazoline)s (POx).

In some examples, where an ASO is linked to a functional moiety, the functional moiety is covalently linked to the ASO. In other examples, the functional moiety is non-
30 covalently linked to the ASO.

Functional moieties can be linked to one or more of any nucleotides in an ASO at any of several positions on the sugar, base or phosphate group, as understood in the art and described in the literature, *e.g.*, using a linker. Linkers can include a bivalent or trivalent branched linker. In some examples, the functional moiety is linked to the 5' end of the ASO. In other examples, the functional moiety is linked to the 3' end of the ASO.

In some examples compositions comprising any of the ASOs disclosed herein also include a delivery nanocarrier complexed with ASO. In some examples, a delivery nanocarrier is selected from among lipoplexes, liposomes, exosomes, inorganic nanoparticles, and DNA nanostructures. In other examples the delivery nanocarrier includes a lipid nanoparticle encapsulating the ASO. Various delivery ASO-nanocarrier complex formats are known in the art, as reviewed in, *e.g.*, Roberts et al., *supra*.

Vectors for Expression of SHANK3 Antisense RNA (AR)

In some examples provided herein is a vector for expression, in a mammalian neuron or other cell type, of an antisense RNA (AR) that binds within a targeted portion of the 3' UTR of a *SHANK3* mRNA; whereby binding of the AR within the targeted portion in a mammalian cell results in an increased level of SHANK3 protein in the mammalian cell.

In some examples, the promoter used in the expression vector is a neuron type-selective promoter for driving expression of the AR in the mammalian cell. In some examples, the neuronal cell type-selective promoter is selective for expression in neurons selected from the list consisting of: cortical, striatal, cerebellar and hippocampal excitatory or inhibitory neurons, including, but not limited to cortical glutamatergic neurons, cortical GABAergic neurons, hippocampal glutamatergic neurons, and striatal inhibitory neurons.

In some the promoter is an inducible promoter, *e.g.*, inducible by a ligand-regulated transactivator such as the tet-inducible rtTA, which allows titration of AR transcription in a target mammalian cell. In some examples, the promoter driving AR expression is a U6 or other Pol III promoter, which is particularly suitable for transcription of short RNA sequences such AR sequences disclosed herein. In some examples, an expression vector utilizes hybrid promoter systems, *e.g.*, a Tet-O-regulated

U6 promoter system as described in Lin et al. (2004), *FEBS Letters*, 577 (2004) 376–380. In some examples, where both cell type-specificity and inducibility of an AR expression vector are desired, a two-part expression system is used in which expression of a ligand-regulated transactivator is driven by a cell type-selective promoter and expression of an AR disclosed herein is driven by a promoter regulated by the ligand-regulated transactivator.

In some examples, the expression vectors used in the compositions disclosed herein are non-viral expression vectors, *e.g.*, plasmid vectors, minicircle DNA vectors, linear amplicon expression cassettes, and the like.

In some examples, composition containing a non-viral expression virus further comprises a transfection agent. Exemplary transfection agents for transfection include, but are not limited to, jet-PEI® (available from Polyplus-transfection® SA, Strasbourg, France); TurboFect in vivo Transfection Reagent (ThermoFisher), and cationic derivatives of polyisoprenoid alcohols (PTAI) as described in, *e.g.*, Rak et al., (2016).

In other examples, the expression vectors to be used are viral vectors, *i.e.*, non-replicative recombinant viruses suitable for expression of an AR disclosed herein.

Preferably, the recombinant virus for expression of the *SHANK3* AR is a DNA virus. Suitable types of DNA viruses include adeno-associated virus (AAV), adenovirus, lentivirus, herpes simplex virus (HSV), and anelloviruses. Methods for design, production, and use of such types of recombinant DNA viruses are established in the art, as exemplified in Fukazawa et al., (2010), *International J of Mol. Med*, 25(1), 3-10, and in "Gene Therapy Protocols" for adenovirus; "Adeno- Associated Virus: Methods and Protocols" for AAV; Cody et al (2013), *Journal of Genetic Syndromes & Gene Therapy*, 4(1), 126, and "Herpes Simplex Virus: Methods and Protocols" for HSV; "Gene Therapy Protocols Vol. 1: Production and In Vivo Applications of Gene Transfer Vectors"; and Merten et al. (2016), *Molecular Therapy – Methods & Clinical Development*, 3, 16017, and Emcagi et al. (2013), *Current Molecular Medicine* 13(4), 602-625 for lentivirus. In some preferred examples, the viral vector is a recombinant AAV.

Genetically Modified Cells

Also provided herein are genetically modified cells. In some examples the genetically modified cells are genetically modified bacterial cells (*e.g.*, recombinant *E. coli*, for amplifying an AR expression vector disclosed herein). In other examples the genetically modified cells are mammalian cells that become genetically modified by virtue of the fact that they have been transfected with any of the ASOs or non-viral AR expression vectors; or transduced with any of the viral AR expression vectors disclosed herein. In some examples, the genetically modified mammalian cells are *ex vivo*, *e.g.*, as a cultured cell population. In other examples, the genetically modified mammalian cells are *in vivo*, *e.g.*, in a mouse. In some examples, the genetically modified mammalian cells are human cells.

In some examples the genetically modified mammalian cells are neurons or neural progenitors. Suitable examples of neurons include, but are not limited to, cortical, striatal, cerebellar and hippocampal excitatory or inhibitory neurons, including, but not limited to cortical glutamatergic neurons, cortical GABAergic neurons, hippocampal glutamatergic neurons, and striatal inhibitory neurons. In some examples such primary cell types can be obtained by differentiation of a human pluripotent stem cell line, *e.g.*, an hiPSC line or a human embryonic stem cell (hESC) line. Methods for obtaining a variety of different neuronal cell types is known in the art, as reviewed in, *e.g.*, Alia et al., (2019), Fitzgerald et al., (2020) and Kim et al., (2014). In other examples, the genetically modified mammalian cells are derived from a cell line. In some examples the cell line is pluripotent stem cell line (*e.g.*, hiPSCs or hESCs) or a neuronal cell line. Suitable neuronal or neuronal stem cell lines include, but are not limited to, SH-SY5Y, NTera, CTX0E16, ReNcell VM, ReNcell Cx. In some preferred examples, the genetically modified mammalian cells express SHANK3 endogenously.

The genetically modified cells disclosed herein can be genetically modified by any of a number of methods and strategies known in the art, *e.g.*, transient transfection, stable transfection, and viral transduction. In some examples transfection with ASOs or non-viral vectors is carried out by nucleofection. In other examples transfection of cells is by lipofection.

Also provided herein are pharmaceutical compositions comprising any of the foregoing ASOs, non-viral expression vectors, and viral expression vectors disclosed herein, and formulated with at least a pharmaceutically acceptable excipient, including a carrier, filler, preservative, adjuvant, solubilizer and/or diluent.

5 Pharmaceutical compositions containing any of the ASOs or expression vector compositions described herein, for use in the methods disclosed herein, can be prepared according to conventional techniques well known in the pharmaceutical industry and described in the published literature. In some examples, a pharmaceutical composition for treating a subject comprises a therapeutically effective amount of any ASO or
10 expression vector disclosed herein.

Pharmaceutically acceptable salts are suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response, *etc.*, and are commensurate with a reasonable benefit/risk ratio. Examples of pharmaceutically acceptable, nontoxic acid addition salts are salts of an amino group
15 formed with inorganic acids such as hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid and perchloric acid or with organic acids such as acetic acid, oxalic acid, maleic acid, tartaric acid, citric acid, succinic acid or malonic acid. Other pharmaceutically acceptable salts include adipate, alginate, ascorbate, aspartate, benzenesulfonate, benzoate, bisulfate, borate, butyrate, camphorate, camphorsulfonate,
20 citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, formate, fumarate, glucoheptonate, glycerophosphate, gluconate, hemisulfate, heptanoate, hexanoate, hydroiodide, 2-hydroxy-ethanesulfonate, lactobionate, lactate, laurate, lauryl sulfate, malate, maleate, malonate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, nitrate, oleate, oxalate, palmitate, pamoate, pectinate, persulfate, 3-
25 phenylpropionate, phosphate, picrate, pivalate, propionate, stearate, succinate, sulfate, tartrate, thiocyanate, p-toluenesulfonate, undecanoate, valerate salts, and the like. Representative alkali or alkaline earth metal salts include sodium, lithium, potassium, calcium, magnesium, and the like. Further pharmaceutically acceptable salts include, when appropriate, nontoxic ammonium, quaternary ammonium, and amine cations
30 formed using counterions such as halide, hydroxide, carboxylate, sulfate, phosphate, nitrate, lower alkyl sulfonate and aryl sulfonate.

In some examples, pharmaceutical compositions are formulated into any of a number of possible dosage routes or forms including, but not limited to, intravenous administration, intrathecal administration, intramuscular administration, tablets, capsules, gel capsules, liquid syrups, and soft gels. In some examples, the compositions are formulated as suspensions in aqueous, non-aqueous or mixed media. Aqueous suspensions may further contain substances that increase the viscosity of the suspension including, for example, sodium carboxymethylcellulose, sorbitol and/or dextran. The suspension may also contain stabilizers. In some examples, a pharmaceutical formulation disclosed herein is provided in a form including, but not limited to, a solution, emulsion, microemulsion, foam or liposome-containing formulation (*e.g.*, cationic or noncationic liposomes).

In some examples, pharmaceutical formulations comprising any of the ASOs or expression vectors described herein may comprise one or more penetration enhancers, carriers, excipients or other active or inactive ingredients as appropriate and known to the skilled person. In some examples, where a pharmaceutical composition includes liposomes, such liposomes can also include sterically stabilized liposomes, *e.g.*, liposomes comprising one or more specialized lipids. These specialized lipids result in liposomes with enhanced circulation lifetimes. In some examples, a sterically stabilized liposome comprises one or more glycolipids or is derivatized with one or more hydrophilic polymers, such as PEG moiety. In some examples, a surfactant is included in the pharmaceutical formulation.

In some examples, a pharmaceutical composition also includes a penetration enhancer to enhance the delivery of ASOs or non-viral expression vectors, *e.g.*, to aid diffusion across cell membranes and /or enhance the permeability of a lipophilic drug. In some examples, the penetration enhancers include a surfactant, a fatty acid, a bile salt, or a chelating agent.

In some examples, where administration is via a systemic route, *e.g.*, intravenous, the method also includes a step to facilitate transfer of any of the ASOs or vectors described herein across the blood brain barrier (BBB) into the CNS, and especially into the brain. In some examples the BBB is transiently disrupted, *e.g.*, by administration of

one or more antibodies that disrupt Netrin-1 binding to Unc5B as described in Boyé et al., (2022).

In some examples, a pharmaceutical composition comprises a dose of ASOs or non-viral vectors ranging from about 0.01 mg/kg to 20 mg/kg, *e.g.*, 0.05 mg/kg, 0.1 mg/kg, 0.2 mg/kg, 0.5 mg/kg, 1 mg/kg, 3 mg/kg, 5 mg/kg, 8 mg/kg, 10 mg/kg, 15 mg/kg, or another dose ranging from about 0.01 mg/kg to 20 mg/kg. In some examples, where an ASO disclosed herein is to be administered directly into the CNS or brain, *e.g.*, by intracerebroventricular administration, the total dose ranges from about 50 mg to about 500 mg, *e.g.*, 60 mg, 70 mg, 80 mg, 100 mg, 120 mg, 150 mg, 180 mg, 200 mg, 220 mg, 250 mg, 270 mg, 290 mg, 300 mg, 350 mg, 400 mg, 450 mg, or another dose from about 50 mg to about 500 mg. This dose range corresponds to approximately 0.050 mg/cm³ of brain volume to about 0.42 mg/cm³ of brain volume assuming an average human brain volume of about 1200 cm³.

In some examples, a pharmaceutical composition comprises multiple ASOs or AR expression vectors. In some examples, a pharmaceutical composition comprises, in addition to ASOs or AR expression vectors, another drug or therapeutic agent suitable for treatment of a subject suffering from *SHANK3* haploinsufficiency.

Methods

As described herein, a number of conditions (*e.g.*, Phelan-McDermid syndrome) are associated with insufficient levels of functional *SHANK3*. Accordingly, the methods described herein include a method for preventing or treating a condition associated with *SHANK3* haploinsufficiency by administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising any of the ASOs or expression vectors disclosed herein. Likewise, in some examples, any of the ASOs or AR expression vectors disclosed herein are used in the manufacture of a medicament for treating a condition associated with *SHANK3* haploinsufficiency. In some examples the condition associated with *SHANK3* haploinsufficiency to be prevented or treated by the methods or with the compositions disclosed herein is Phelan-McDermid syndrome, an autism spectrum disorder, schizophrenia, or an intellectual disability. In some preferred examples, the condition is Phelan-McDermid syndrome.

Also provided herein is a method for increasing the amount of functional SHANK3 protein in a mammalian cell expressing *SHANK3* mRNA, the method comprising contacting the cell with any of the ASOs or expression vectors disclosed herein.

5 In some examples, administration to a subject or contact with cells *in vitro* or *ex vivo* with any of the ASOs, AR expression vectors, or pharmaceutical compositions disclosed herein increases the level of SHANK3 protein about 1.1 to about 5 fold in cells (*e.g.*, neurons) *in vitro* or *ex vivo*, *e.g.*, 1.2 fold, 1.3 fold, 1.5 fold, 1.7 fold, 2 fold, 2.2 fold, 2.5 fold, 2.7 fold, 3 fold, 3.3 fold, 3.5 fold, 4 fold, 4.3 fold, 4.5 fold, 4.7 fold, or
10 another increase in SHANK3 protein levels from about 1.1 fold to about 5 fold in cells in a subject or *in vitro* or *in vivo*.

Suitable routes of administration for treatment with the compositions, pharmaceutical compositions, or medicaments disclosed herein include, but are not limited to, intravenous, intra-arterial, intraparenchymal, intracerebroventricular, intra-
15 cisterna magna, intrathecal, intravenous, intra-arterial, subcutaneous, and topical.

As the skilled person will understand, the treatment methods disclosed herein include administration of the compositions and pharmaceutical compositions disclosed herein in a therapeutically effective amount to a subject (*e.g.*, a human subject). The terms "effective amount" or "therapeutically effective amount," as used herein, refer to a
20 sufficient amount of a disclosed ASO, non-viral or viral expression vector being administered to relieve to some extent one or more of the symptoms and/or clinical indicia associated with SHANK3 haploinsufficiency in a particular disease or health condition. In some examples, an "effective amount" for therapeutic uses is the amount of one of the foregoing agents required to provide a clinically significant decrease in
25 disease symptoms to prevent disease symptoms without undue adverse side effects. Examples of suitable symptoms to be reduced by the treatment methods provided herein included, but are not limited to, seizures, anxiety, repetitive behaviors, learning and memory deficits, and impaired sociability. An appropriate "effective amount" in any individual case may be determined using techniques, such as a dose escalation study.
30 The term "therapeutically effective amount" includes, for example, a prophylactically effective amount. It is understood that "an effective amount" or "a therapeutically

effective amount" can vary from subject to subject, due to variation in metabolism of the compound of any age, weight, general condition of the subject, the condition being treated, the severity of the condition being treated, and the judgment of the prescribing physician. By way of example only, therapeutically effective amounts may be determined by routine experimentation, including but not limited to a dose escalation clinical trial. Where more than one therapeutic agent is used in combination, a "therapeutically effective amount" of each therapeutic agent can refer to an amount of the therapeutic agent that would be therapeutically effective when used on its own, or may refer to a reduced amount that is therapeutically effective by virtue of its combination with one or more additional therapeutic agents.

Combination Treatments

The pharmaceutical compositions comprising any of the ASOs or AR expression vectors, disclosed herein, can also be used in combination with other agents of therapeutic value in the treatment of a condition associated with SHANK3 haploinsufficiency. In general, other agents do not necessarily have to be administered in the same pharmaceutical composition, and may, because of different physical and chemical characteristics, preferably be administered by different routes. The determination of the mode of administration and the advisability of administration, where possible, in the same pharmaceutical composition, is well within the knowledge of the skilled clinician. The initial administration can be made according to established protocols known in the art, and then, based upon the observed effects, the dosage, modes of administration and times of administration can be modified by the skilled clinician.

Compositions and pharmaceutical compositions comprising ASOs and/or expression vectors, and an additional therapeutic agent may be administered concurrently (*e.g.*, simultaneously, essentially simultaneously or within the same treatment protocol) or sequentially, depending upon the stage and progression of the SHANK3 haploinsufficiency-associated condition to be treated, the condition of the patient, and the choice of specific therapeutic agents used. The determination of the order of administration, and the number of repetitions of administration of each therapeutic agent

during a treatment protocol, is well within the knowledge of the skilled physician after evaluation of the disease being treated and the condition of the patient.

It is known to those of skill in the art that therapeutically-effective dosages can vary when the drugs are used in treatment combinations. Methods for experimentally determining therapeutically-effective dosages of drugs and other agents for use in combination treatment regimens are described in the literature. For example, the use of metronomic dosing, *i.e.*, providing more frequent, lower doses in order to minimize toxic side effects, has been described extensively in the literature. Combination treatment further includes periodic treatments that start and stop at various times to assist with the clinical management of the patient.

For combination therapies, dosages of co-administered therapeutic agents will of course vary depending on the type of co-agents employed, ASO or expression vector, and the disease stage of the patient to be treated.

Pharmaceutical compositions comprising ASOs, ARs, or expression vectors, and an additional therapeutic agent that make up a combination therapy disclosed herein may be a combined dosage form or in separate dosage forms intended for substantially simultaneous administration. The pharmaceutical compositions that make up the combination therapy may also be administered sequentially, with either therapeutic agent being administered by a regimen calling for two-step administration. The two-step administration regimen may call for sequential administration of the active agents or spaced-apart administration of the separate active agents. The time period between the multiple administration steps may range from, a few minutes to several hours, depending upon the properties of each pharmaceutical agent, such as potency, solubility, bioavailability, plasma half-life and kinetic profile of the pharmaceutical agent. Circadian variation of various physiological parameters may also be evaluated to determine the optimal dose interval.

Examples of suitable therapeutic agents for co-administration with a composition or a pharmaceutical composition disclosed herein include, but are not limited to, Growth Hormone, Insulin-Like Growth Factor-1, Risperidone, Lumateperone, sodium valproate, lithium, and D-serine.

EXAMPLES

Example 1: Identification of *SHANK3* Target Sequences in the 3' UTR.

ASO sequences are designed as 1 nucleotide microwalks of *SHANK3* 3' UTR target regions of interest. Matured sequences are generated to optimize therapeutic outcomes utilizing two approaches; employment of advanced algorithms to design mismatches that improve the ASO's neurotoxicity score and systematically introduce mismatches to enhance general tolerability and manufacturability. The resulting ASO sequences correspond to **SEQ ID NOs:3-1078**, which are provided in Table 1 (Appendix) and in the accompanying sequence listing; and **SEQ ID NOs:16254-18750** provided in the accompanying sequence listing. Figure 1 illustrates a potential mechanism of antisense oligonucleotides by masking binding sites for miRNAs (e.g., a binding site for miR-504) located within the *SHANK3* mRNA 3' UTR and prevent access of these miRNAs to their binding sites, thereby resulting in an increased level of *SHANK3* gene expression. For RNA seq analysis of *SHANK3* mRNA and miR-504, bulk-RNA-seq raw data was downloaded from the publicly available BrainSpan data repository. Fastq files were quality checked and adapter trimmed using the fastp tool. Then, processed reads were mapped against the T2T genome reference and the lift off gene annotation from Gencode v45. Transcript quantification was performed with Salmon tool using the same lift off gene annotation mentioned before. Transcript quantification was transformed to gene counts using the tximeta R tool. Gene expression analysis was performed in R with edgeR. Samples with ≤ 10 million reads were discarded, and data was normalized with the TMM edgeR method. MicroRNA filtered counts from the BrainSpan Small RNA-seq data was obtained from PsychENCODE processed data repository. MicroRNA counts were normalized and expression analysed using edgeR tool in R. Figure 2 demonstrates the expression of miR-504 (hsa-mir-504-5p) and *SHANK3* mRNA expression in human brain samples by RNAseq.

Example 2: Screening of peptide-conjugated phosphorodiamidate morpholinos (PPMOs) in a neuronal cell line.

PMO sequences corresponding to (**SEQ ID NOs:160, 327, 369, 637, and 687**) in Example 1 were conjugated to a cell penetrating peptide (**SEQ ID NO: 2**) to generate

PPMOs and assessed in SH-SY5Y cells for their ability to increase SHANK3 protein expression levels. PPMO were applied to SH-SY5Y neuronal cell line cultures at concentrations of 5 μ M and 10 μ M and incubated for 5 days. Five days after PPMO treatment, total protein was extracted on ice using RIPA buffer supplemented with 1% protease inhibitor cocktail (Sigma, cat no P8340) and 1x PhosSTOP (Sigma, cat no 4906837001). Protein lysates were cleared by centrifugation, and total protein was quantitated using BCA protein kits (ThermoFisher Scientific, cat no 23225). Expression levels of SHANK3 protein were quantified by Enzyme Linked Immunosorbent Assay (ELISA). Samples were diluted in phosphate buffered saline (PBS), pH 7.4 (1 part lysate + 19 parts PBS) and further diluted in 5% RIPA buffer in PBS as necessary, and standard curves were prepared in 5% RIPA buffer in PBS to match. Diluted samples and standards were loaded onto pre-coated human SHANK3 ELISA plates, and the assays were performed as directed by the manufacturer (FineTest, Cat no. EH4462). The absorbances at 450 nm were measured using a VICTOR[®] Nivo[™] multimode plate reader, and quantitative analysis was performed using GraphPad Prism Ver 10.2.3 software. A non-targeting control, predicted not to hybridize to human transcripts, was included as a negative control. Results were first normalized to total protein concentration and then expressed as fold-change relative to untreated cells (UT). Figure 3 demonstrates the efficacy of PPMOs in inducing SHANK3 protein upregulation. The results showed that the PPMO having an oligonucleotide sequence corresponding to **SEQ ID NO:687** significantly upregulates SHANK3 protein up to two fold in SH-SY5Y cells.

Example 3: Effect of a selected PPMO on SHANK3 protein levels in human iPSC-derived neurons.

A peptide-conjugated PMO (PPMO) having the nucleotide sequence corresponding to **SEQ ID NO:160** was selected to test its efficacy in iPSC-derived glutamatergic neurons derived from a healthy control subject (Cell ID: 1332iso). The iPSC-derived glutamatergic neurons were incubated with the PPMO for seven days. At day 7 post-treatment, total protein was extracted, cleared, and quantified as previously described in Example 2. The upregulation level of SHANK3 protein was quantitated using Enzyme Linked Immunosorbent Assay (ELISA). Samples were pre-diluted in

phosphate buffered saline (PBS), pH 7.4 (1 part lysate + 19 parts PBS) and standard curves were prepared in 5% RIPA buffer in PBS to match. Diluted samples and standards were loaded onto pre-coated human SHANK3 ELISA plates, and the assays were performed as directed by the manufacturer (FineTest, cat no EH4462). The absorbances at 450 nm were measured using a VICTOR® Nivo™ multimode plate reader, and quantitative analysis was performed using GraphPad Prism Ver 10.2.3 software. A non-targeting control, predicted not to hybridize to human transcripts, was included as a negative control. Results were first normalized to total protein concentration and then expressed as fold-change relative to UT. Figure 4 present the assessment of SHANK3 protein expression at day 7 post PPMO treatment. The results demonstrate 1.3 fold SHANK3 protein upregulation following 10 µM PPMO treatment in iPSC-derived glutamatergic neurons.

In a subsequent experiment, a PPMO having an oligonucleotide sequence corresponding to SEQ ID NO:1847 disclosed in WO 2023/235915, and having CPP as in examples above (SEQ ID NO:2) was tested in Phelan-McDermid Syndrome (PMS) patient hiPSC-derived glutamatergic neurons. The PPMO was incubated with iPSC-derived glutamatergic neurons in triplicate for 7 days. A non-targeting control, predicted not to hybridize to human transcripts, was included as a negative control. Figure 5 shows a bar graph representing mean+S.D. of SHANK3 protein normalized to total protein amount loaded relative that of untreated cells. n=1 biological replicate. UT = untreated cells. Graph was generated using GraphPad Prism Ver 10.2.3 software. *p<0.05, **p<0.005, ***p<0.001. One-Way ANOVA. The PPMO was found to increase levels of SHANK3 protein in PMS glutamatergic neurons to a level similar to those found in control neurons.

SHANK3 has six main isoforms encoded by six different promoters located along the gene. There are five main isoforms well characterized in the brain including a, c, d, e and f (Monteiro et al., 2017). SHANK3 protein isoform 'a' is the full length protein of ~185 kDa and contains the six main SHANK3 functional protein domains: (1) SHANK/ProSAP N-terminal (SPN) domain interacts with small GTPases of the Ras superfamily involved in the regulation of synaptic F-actin structure and dynamics and in postsynaptic signal transduction; (2) Ankyrin repeat (ANK) region binds the cytoskeletal

protein α -fodrin, an adhesive junction associated protein δ -catenin, and a component of a ubiquitin ligase complex, sharpin; (3) Src homology 3 (SH3) domain directly associates with the Ca^{2+} channel Ca1.3; (4) PSD-95/DLG/ZO-1 (PDZ) domain is involved in a direct interaction with SAPAP1 or the GluA1 subunit of AMPA receptors; (5) Proline-rich (Pro) region harbors multiple protein interaction sites including those for homer1 and cortactin, relevant for linking of SHANK3 to other PSD scaffolds and the regulation of spinous actin dynamics; (6) Sterile alpha motif (SAM) domain facilitates oligomerization of SHANK3 within the postsynaptic density (PSD) and is required for postsynaptic targeting. SHANK3 isoform 'c' contains the last four proteins domains, SH3, PDZ, Pro and SAM domains, and has a mass of ~140 kDa. SHANK3 protein isoform 'd' has the last three protein domains (PDZ, Pro and SAM) and a mass ~127 kDa. SHANK3 protein isoform 'e' only carries the two last protein domain (Pro and SAM) and has a mass of ~118 kDa. Finally, SHANK3 protein isoform 'f' starts within the Pro domain and includes the SAM domain, making a mass ~88 kDa. The isoforms described above are the main isoform models for a, c, d, e and f, however there are some variants of these ones with and without internal exons (Monteiro et al., *supra*. The molecular weight (MW) of each isoform can vary due to these isoform variants and post-transcriptional modification.

Thus, in order to assess the effect of one ASO on expression levels of some separate SHANK3 isoforms, a subsequent experiment, an ASO having the sequence corresponding to SEQ ID NO:1193 disclosed in WO 2023/235915 was tested in commercially available human iPSC-derived glutamatergic neurons (cat no: io1001, bit.bio) to determine the effect of this ASO on various SHANK3 isoforms known to be expressed in glutamatergic neurons. The iPSC-derived glutamatergic neurons were transfected with the ASO at 0.125 μM and 0.25 μM using ViaFect™ Transfection Reagent (cat no: E4981, Promega) and incubated for seven days. At day 7 post-treatment, total protein was extracted, cleared, and quantified. The upregulation level of SHANK3 protein isoforms was assessed using western blot assay. On day 7 post-treatment, protein was extracted on ice using RIPA buffer supplemented with 1% protease inhibitor cocktail (Sigma, cat no P8340) and 1x PhosSTOP (Sigma, cat no 4906837001). Protein lysates were cleared by centrifugation, and total protein was quantitated using BCA protein kits

(ThermoFisher Scientific, cat no 23225). Samples were prepared by the addition of 1x Laemmli sample buffer (Bio-Rad, cat no 1610747) and Bond-Breaker™ TCEP (ThermoFisher Scientific, cat no 77720), boiled to denature proteins, then separated on NuPAGE™ 4 to 12% Bis-Tris protein gels (Invitrogen, cat no WG1401BOX). Protein
5 was transferred to 0.2 µm nitrocellulose membranes (Bio-Rad, cat no 162112) by wet transfer overnight at 4°C. The membrane was stained for total protein (Licor, cat no 926-11021) and rabbit monoclonal anti-SHANK3 primary antibody (Cell Signaling Technology, cat no 64555S) followed by anti-rabbit secondary antibody (IRDye® 800CW preabsorbed, Abcam, cat no ab216773). Blots were imaged on an Odyssey
10 Imager, and quantitative analysis was performed using Image Studio Ver 5.5 software. The raw fluorescence signal for each SHANK3 protein isoform was first normalized to the raw fluorescence signal of loading control (total protein). The expression level of the normalized SHANK3 protein isoform was compared to the one of the untreated control, which was set as the baseline value of 1. The expression level of the normalized
15 SHANK3 protein isoforms was compared to those of the untreated control, which were set as the baseline value of 1. Figure 6 shows the assessment of SHANK3 isoform protein expression at day 7 post ASO treatment determined by western blot assay. The results demonstrate approximately 1.2-1.5 fold upregulation of major SHANK3 isoforms a, c/d. Thus, while levels of each of the major isoforms evaluated were increased, the relative
20 ratio of expression levels between the essential isoforms appears unchanged.

Example 4: Design for the maturation of 2'MOE ASO sequences targeting the 3'UTR of SHANK3 transcript

The 2'-O-methoxyethyl (2'MOE) sequences that target the SHANK3 transcript
25 adjacent to and within the hsa-miR-504 seed sequence (SEQ ID NO: 1079) were further refined by adjusting their length (15-, 16-, 18- and 20-mers) and/or refining their target sequence to reduce GC content and improve neurotoxicity profiles. The resulting ASO sequences correspond to SEQ ID NOs:1080-1093, which are provided in Table 2 and are illustrated in Figure 7C. Figure 7 shows the binding sites within the target mRNA
30 region (SEQ ID NO:1079) for ASOs with SEQ ID NOs: 1094 and 1095 (herein) which are originally disclosed in WO 2023/235915 as SEQ ID NO:1193 ("MOE55") and

SEQ ID NO:1847 (“PMO40”), respectively. ASO sequences corresponding to SEQ ID NOs.: 1080-1093, are provided in Table 2 and are illustrated in Figure 7.

Example 5: Screening of 2'MOE ASOs targeting the 3'UTR of the SHANK3 transcript

2'-O-methoxyethyl (2'MOE) ASOs corresponding to SEQ ID NOs: 800, 817, 826, 856, 879, 954, 1015, and 1080-1094 were tested to assess their ability to increase SHANK3 protein expression levels. ASOs were transfected at concentrations of 0.5 μ M and 1 μ M to commercial iPSC-derived Cortical Glutamatergic Neurons (Cat. No. BX-0300-30, BrainXell) using ViaFect Transfection Reagent (Cat no. E4982, Promega). Additionally, a non-targeting control, predicted not to hybridize to human transcripts, was included as a negative control. Seven days after 2'MOE treatment, total protein was extracted, cleared, and quantified as described in Example 2. Expression levels of SHANK3 were assessed following the protocols described in Example 3. Figure 8 presents the assessment of SHANK3 protein expression in commercial iPSC-derived glutamatergic neurons (Cat. No. BX-0300-30, BrainXells) at day 7 post 2'MOE treatment (n=1 biological replicate; n=3 technical replicates). The results demonstrate that ASOs with SEQ ID NOs: 954, 1092, 1094, 1086, and 1087 increased the expression of SHANK3 protein by $\geq$ 1.3-fold at 0.5 μ M. Additionally, ASOs SEQ ID NOs.: 954, 1091, 1092, 1094, 1087 and 1088 showed a $\geq$ 1.3-fold SHANK3 protein upregulation at 1 μ M treatment in commercial iPSC-derived glutamatergic neurons (Cat. No. BX-0300-30, BrainXells). Furthermore, ASOs with SEQ ID NOs: 1085, 1089, 879, and 1084 showed a slight increased level of SHANK3 protein ($\geq$ 1.1) at one or both concentrations.

Example 6: Gymnotic screening of selected 2'MOE ASOs on SHANK3 protein levels in human iPSC-derived neurons

Based on the results from Example 5, six ASO sequences (SEQ ID NOs: 1084, 1087, 1091, 1092, 1093, and 1094) were selected for screening in commercial iPSC-derived glutamatergic neurons (Cat. No. BX-0300-30, BrainXells) via gymnotosis. In brief, ASOs with SEQ ID NOs: 1084, 1087, 1091, 1092, 1093, and 1094 were directly

incubated with iPSC-derived glutamatergic neurons at concentrations of 7.5 μ M, 15 μ M, and 30 μ M. At 14-day post treatment, total protein was harvested as described in Example 2 and SHANK3 protein expression levels were determined as described in Example 3. **Figure 9** illustrates the effect of the selected 2'MOE on SHANK3 protein levels in human iPSC-derived neurons (n=1 biological replicate; n=3 technical replicates). In some test cases (**SEQ ID NOs: 1091, 1084, 1094, and 1087**) 2'MOE treatment demonstrated a ≥ 1.3 fold SHANK3 protein upregulation at 7.5 μ M treatment in commercial iPSC-derived glutamatergic neurons (Cat. No. BX-0300-30, BrainXells). In some other cases (**SEQ ID NOs: 1084, 1094, and 1087**) 2'MOE treatment demonstrated a ≥ 1.3 fold SHANK3 protein upregulation at 15 μ M treatment in commercial iPSC-derived glutamatergic neurons (Cat. No. BX-0300-30, BrainXells). In some other cases (**SEQ ID NOs: 1091, 1092, and 1094**) 2'MOE treatment demonstrated a ≥ 1.3 fold SHANK3 protein upregulation at 30 μ M treatment in commercial iPSC-derived glutamatergic neurons (Cat. No. BX-0300-30, BrainXells). ASOs with **SEQ ID NOs: 1091, 1092, 1084, 1094, and 1087** showed a slightly increased level of SHANK3 protein (≥ 1.1) at one or both concentrations. The differences in protein upregulation fold change between **Figure 8** and **Figure 9** may be attributed to the transfection efficiency of each ASO, whether delivered with the transfection reagent or via gymnosis.

Example 7: Chemical modification of selected MOEs to optimize ASOs for increased SHANK3 protein expression.

Locked nucleic acids (LNAs) were incorporated into the selected 2'MOE ASO sequences (**SEQ ID NOs: 1084, 1087, 1091, 1092, 1093, and 1094**) from Example 6 in order to increase their potency and specificity. Each ASO sequence (**SEQ ID NOs: 1096-1103, 1107, 1111, 1112, 1119, 1120, 1125, and 1132**) was designed with the addition of two or three LNAs. In these cases, LNAs were either distributed to divide the ASO into equal parts, or placed in specific nucleotides that have mismatches to potential off-target sequences, reducing the likelihood of the ASO to hybridize in a stable manner to off-target mRNA sequences. Additionally, one or two nucleotides within the parental ASO sequences (**SEQ ID NOs: 1084, 1087, 1091, 1092, 1093, and 1094**) were replaced by abasic spacers. To account for the loss of binding strength when using abasic spacers,

ASO sequences including abasic spacers (SEQ ID NOs: 1104-1106, 1108-1110, 1113-1118, 1121-1124, 1126-1131 and 1133) comprise one or two LNAs on the nucleotides flanking an abasic spacer. Abasic spacers were included to reduce the GC content of the parental ASO sequences (SEQ ID NOs: 1084, 1087, 1091, 1092, 1093, and 1094) to improve their tolerability and manufacturing. All ASO sequences designed with LNAs and LNAs with abasic spacers are listed in Table 3, in which LNA modified nucleotides are denoted by a "*" and abasic spacers with an "S".

Example 8: Effect of selected derivatized MOEs on SHANK3 protein levels in human iPSC- derived neurons.

LNA modified 2'MOE ASOs (SEQ ID NOs:1096-1133) were screened in commercial iPSC-derived glutamatergic neurons (Cat. No. BX-0300-30, BrainXells) via gymnosis. ASOs were directly added to the media of seeded cells at three doses: 7.5 μ M, 15 μ M and 30 μ M. Total protein was harvested at day 14 post-treatment as described in Example 2 and SHANK3 protein upregulation was determined as stated in Example 3. Figure 10 illustrates the effect of LNA modified ASO sequences on SHANK3 protein levels in commercial iPSC-derived glutamatergic neurons (Cat. No. BX-0300-30, BrainXells) transfected via gymnosis (n=1 biological replicate; n=3 technical replicates). The bar plots represent the mean $\pm$ SD of SHANK3 protein normalized to the total protein loaded, relative to the normalized SHANK3 protein of untreated cells. White bar plots correspond to untreated cell controls (UT) and non-targeting control (NTC); light gray, dark gray, and black bars represent cells treated with ASO at 7.5 μ M, 15 μ M and 30 μ M, respectively. Figure 10A shows the screening of derivatives from three parental 18-mer ASO sequences (SEQ ID NOs: 1091, 1093, and 1092). In some cases, ASO sequences achieved ≥ 1.3 fold at 7.5 μ M (SEQ ID NOs: 1115, 1119, and 1122). In some other cases, ASO sequences achieved ≥ 1.3 fold at 15 μ M (SEQ ID NOs: 1127 and 1128). In some other cases, ASO sequences achieved ≥ 1.3 fold at 30 μ M (SEQ ID NO: 1121). In some other cases, ASO sequences with SEQ ID NOs: 1114, 1119, 1120, 1121, 1122, 1123, 1125, and 1127 presented a slight increase of SHANK3 protein of ≥ 1.1 -fold change. Figure 10B shows the screening of derivatives from three parental ASO sequences of diverse lengths 15-mer (SEQ ID NO:1084), 17-mer (SEQ ID NO:1094) and 20-mer

(SEQ ID NO:1087). In some cases, ASO sequences achieved ≥ 1.3 fold at 7.5 μM (SEQ ID NOs:1096, 1103, 1109, and 1111-1113). In some other cases, ASO sequences achieved 1.3 fold at 15 μM (SEQ ID NO.: 1096, 1103, 1109-1111 and 1104-1106). In some other cases, ASO sequences achieved ≥ 1.3 fold at 30 μM (SEQ ID NOs: 1096, 1103, 1109-1111, and 1113). In some other cases, ASO sequences with SEQ ID NO: 1097, 1100, 1102, and 1107 presented a slight increase of SHANK3 protein of ≥ 1.1 -fold change.

Example 9: Effect of selected MOEs on SHANK3 protein levels in human iPSC-derived neurons from Phelan-McDermid Syndrome patients.

2'MOE ASOs having the nucleotide sequence corresponding to SEQ ID NOs: 1094, 1087, 1091, 1093 and 1092 were screened to test their efficacy in increasing SHANK3 protein in iPSC-derived glutamatergic neurons derived from a Phelan-McDermid Syndrome patient (PMS patient #1) via gymnotic uptake. ASOs were directly added to the media of cultured cells at four concentrations: 7.5 μM , 15 μM , 30 μM and 45 μM . Total protein was harvested at day 14 post-treatment as described in Example 2 and SHANK3 protein upregulation was determined as stated in Example 3. **Figure 11A** illustrates the effect of tested ASOs on SHANK3 protein levels in iPSC-derived glutamatergic neurons derived from a Phelan-McDermid Syndrome patient transfected via gymnosis (nN=1 biological replicate; n=3 technical replicates). In some cases, ASO treatment (SEQ ID NOs: 1094, 1087 and 1092) significantly increased ≥ 1.5 -fold SHANK3 protein at an ASO concentration of 7.5 μM . In some cases, ASO treatment (SEQ ID NOs: 1094, 1087, 1091 and 1092) significantly increased ≥ 1.5 -fold SHANK3 protein at an ASO concentration of 15 μM . In some cases, ASO treatment (SEQ ID NOs: 1094, 1087, 1091, 1093 and 1092) significantly increased ≥ 1.5 -fold SHANK3 protein at an ASO concentration of 30 μM . In some cases, ASO treatment (SEQ ID NOs: 1094, 1087 and 1092) significantly increased ≥ 1.5 -fold SHANK3 protein at an ASO concentration of 45 μM . In some cases, ASO treatment (SEQ ID NOs: 1094, 1087, 1091, 1093 and 1092) increased ≥ 1.3 -fold SHANK3 protein at three or all ASO concentrations tested. In some cases, ASO treatment (SEQ ID NOs: 1094, 1087, 1091, 1093 and 1092) increased ≥ 1.1 -fold SHANK3 protein at all ASO concentrations tested.

A subsequent experiment was conducted with LNA-modified and fully 2'MOE parental ASOs having nucleotide sequences corresponding to **SEQ ID NOs: 1122, 1093, 1126, 1128, and 1092**. These ASOs were tested for their efficacy in iPSC-derived glutamatergic neurons from a Phelan-McDermid Syndrome patient (PMS patient #1) via gymnotic uptake. ASOs were incubated directly with cells at three concentrations: 7.5 μ M, 15 μ M and 30 μ M. Parental ASO sequences with **SEQ ID NOs: 1092 and 1093** were applied only at 30 μ M. Total protein was harvested at day 14 post-treatment as described in Example 2, and SHANK3 protein upregulation was assessed as outlined in Example 3. **Figure 11B** illustrates the effect of tested ASOs on SHANK3 protein levels in iPSC-derived glutamatergic neurons derived from a Phelan-McDermid Syndrome patient transfected via gymnotic (n=1 biological replicate; n=3 technical replicates). In all cases and concentrations tested, ASO sequences (**SEQ ID NOs: 1122, 1093, 1126, 1128, and 1092**) achieved ≥ 1.5 -fold change of SHANK3 protein upregulation over untreated cells. Significance of the fold change was calculated with a one-way ANOVA test where (*) denotes a p. adj < 0.05 , (**) a p. adj < 0.01 , (***) a p. adj < 0.005 and (****) a p. adj < 0.001 .

Example 10: Effect of selected MOEs on SHANK3 protein levels in human iPSC-derived neurons from Phelan-McDermid Syndrome patients.

Spontaneous calcium oscillations have been shown to be impaired in PMS patient-derived neurons compared to unaffected control neurons (Darville, et al. 2016). To investigate whether PMS patient iPSC-derived neurons in this study show similar impairments in neuronal function, calcium oscillation activity was assessed in two independent PMS patient lines (PMS patient #1 and #2) compared to two non-PMS (non-SHANK3-deficient) control lines. In brief, intracellular calcium was measured with Fluo-4 Direct™ (cat no. F10471, ThermoFisher) following manufacture's protocol, and plates were incubated at 37 °C for 60 min. Plates were read on CLARIOstar (software version 5.70 R3) with fluorescence mode at 494/516 nm (ex/em) for 1 minute at 0.1 sec intervals. Raw data was pre-processed in R program adapted from Per Uhlen, 2004 for Spectral Analysis of Calcium Oscillations, in which a trend correction and catering of the signal is performed followed by normalizing the data to frequency to obtain the power

spectral density, referred as signal intensity. Signal intensities lower than the mean signal intensity from blanks (wells without cells) were filter out. Remaining data was used to calculate the median signal intensity for each sample and condition. **Figure 12A** illustrates the signal intensity baseline of the calcium oscillations in two PMS patient and two non-PMS control iPSC-derived glutamatergic neurons (commercial BrainXells and donor iPSC). The bar plots are divided in two sets, one for each PMS cell line, as PMS patient #1 together with its non-PMS controls was seeded at 25,000 – 30,000 cells per well, while the set of PMS patient #2 at 10,000 cells per well. Both PMS patient lines show a decreased signal intensity compared to both SHANK3-non-deficient lines. To test whether increased SHANK3 protein following ASO treatment resulted in increased neuronal activity in Phelan-McDermid patient iPSC-derived glutamatergic neurons (PMS patient #1), calcium oscillations were assessed 21 days post gymnotic ASO treatment. In brief, iPSC-derived neurons were single-dose treated with 2'MOE_s corresponding to **SEQ ID NOs: 1094, 1091, 1092, 1087, and 1093** at 15 μ M and 30 μ M and assessed 21 days post-treatment (**Figure 12B**). Additionally, a double-dose treatment with **SEQ ID NOs:1094, 1091, 1092, 1087 and 1093** was performed for the 15 μ M, 7 days after the first treatment (**Figure 12C**). At day 21 post-treatment, intracellular calcium was measured and analysed as described above. Untreated ASO wells were incubated for 60 minutes with BAPTA-AM, as a negative control, at 20 μ M (Cat no. B1205, Invitrogen); or positive control Ionomycin at 1 μ M (Cat no. I24222, Invitrogen) prior to plate reading (**Figure 12C**). **Figure 12B** illustrates the change in the signal intensity of the calcium oscillations as a response to the single-dose gymnotic ASO treatment at 15 μ M and 30 μ M, day-21 post treatment. All ASO treatments with **SEQ ID NO: 1094, 1091, 1092, 1087 and 1093** increased (≥ 1.1 -fold change) calcium oscillations signal intensity compared to PMS untreated cells. **Figure 12C** illustrates the change in the signal intensity of the calcium oscillations as a response to the double-dose gymnotic ASO treatment at 15 μ M on day-21 post treatment. ASO treatment with **SEQ ID NO: 1094, 1091 and 1092** increased (≥ 1.1 -fold change) the signal intensity of calcium oscillations compared to PMS untreated cells.

Example 11: Identification of *SHANK3* Target Sequences

Identification of annotated and expressed transcripts that could generate the canonical transcript of the *SHANK3* gene was performed by the sequence alignment of all *SHANK3* protein-coding and NMD transcripts described in Gencode v38. An ASO sequence “micro-walk” of 18mers and 25-mers in 1 bp increments was performed over the sequences of intron 7, 17, and 21 of the **ENST00000262795.6** pre-mRNA transcript and designed to target the intronic splice enhancer motif to mediate exclusion of the retained intron or part thereof and generate productive *SHANK3* mRNA transcript. The resulting ASO sequences correspond to **SEQ ID NOs:4584-11700** provided in the accompanying sequence listing (incorporated by reference herein).

It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the invention as shown in the specific examples without departing from the spirit or scope of the invention as broadly described. The present examples are, therefore, to be considered in all respects as illustrative and not restrictive.

This application claims priority from:

Australian Provisional Application No. 2023903841 filed on 29 November 2023;
Australian Provisional Application No. 2023903842 filed on 29 November 2023;
Australian Provisional Application No. 2023903916 filed on 4 December 2023;
Australian Provisional Application No. 2023903924 filed on 5 December 2023;
Australian Provisional Application No. 2023903927 filed on 6 June 2024;
Australian Provisional Application No. 2024901708 filed on 6 June 2024,
Australian Provisional Application No. 2024902223 filed on 17 July 2024; and
Australian Provisional Application No. 2024903714 filed on 13 November 2024, the entire contents of each of which are hereby incorporated by reference in their entirety.

All publications cited herein are hereby incorporated by reference in their entirety. Where reference is made to a URL or other such identifier or address, it is understood that such identifiers can change and particular information on the internet can come and

go, but equivalent information can be found by searching the internet. Reference thereto evidences the availability and public dissemination of such information.

Any discussion of documents, acts, materials, devices, articles or the like that have been included in the present specification is solely for the purpose of providing a context
5 for the present invention. It is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed before the priority date of each claim of this application.

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Appendix: Sequences and SEQ ID NOs

SEQ ID NO:1

5 *SHANK3* mRNA Canonical Transcript 3' UTR Sequence (from *SHANK3*-201
ENST00000262795.7)

CGCCCCACCCCCACTCCCCGCCCCGGCCGTGCCCTGCCGGCAGGGCCCCCACCCCCACCC
CGGGCCCGGGGCTCGGCCCTGCCCTTACGACGGCGCCCGGGCCAGGAATGTTGCATGAAT
10 CGTCCTGTTTGCTGTTGCTCGGAGACTCGCCCTGTACATTGCTTAGTGCCCTCACCGGCC
GCCCAGCCCCACCCAGCGCACAGTCAGGAAGGGCGTGGACCAGGGAGGCTGGGGCGGGAGG
TGCCGGGGGTGGGGTGCCCTAGCGTGACCACCTCCTTCGCAGCTCCTGGTGCCATTCTC
CCAGAGGGGGAACCTAGTCCAGCATGCGAGGTGAGGACCCGCTTGGTGACTCGGGGGGA
GGGGGGAGACATTGGGATTCTCGATGGGGGCCAAGGAGCCCCCTGTTTGCATATTTTA
15 ATCCACTCTATATTGGAACGAGAAAAGGAACAAATATCTGTCCGTAATAGTTTCCTC
TCCCTCCCTTCTACTTCCACTGGTCCCACTGCAGCTGCCAGTCTCCATCTCCGGCCC
CTCACTGCCACTGCCACCCACAACGGGGCAGGGGACGCTCCAGCTGGTCTGGGGTTGGC
CAGGGCCCTAGTGGCCCGCCCTGGGGCCCCAGCTCGGCCCTCGCCTCGCTGAGCTCTAG
TGTGCCCCACCGACCTTCAGGTGCTGCTCGTGTTGGAGGGGCGGCAGGCCGCGGGTCC
20 TGCTGTGCACCCGCGGGACCAGCCGGCCTGGGAGACCATCGGCCGGGGGGGATGAGGGCA
GGGCCCTGCCGCTCCACCGCAGCCATCTTCCTCACAGGGTCTCTCCCAAGGAGGGGGCT
AGCTTGGTCCCCATGCTCTTGGGCACTACAGCAGAGAAGCCTCCCTGCCTTGGACCCCA
AAGTCTCCTGTCTGCCCTTTATGTGTGTGGGTGAACTGGGTGCGTCTGAGCACGTGGG
AGCCGTGTGTGTGCCTGATTACTGAGTGCCACCAGGGGCCGCTCTGGACTAGCGGGGG
25 CCGTGGAGGGCTGCACCGTGTGCATGCGTGGGGTGTACCTGTGAGAGCACCTGTCTCCT
CTTCCAAAGAAAGTCAGAGGCCATCCTGCACCCCTGGGTCCAGCTGTTTGCCAGCCTGTC
CTTCCAGAGCCTCACCCAGCCTGAGCGGGGTTCCTGGTGAATCCCTGCTGCTTGGGGAG
GCCCCAAGGGCCCCTTGGAGGCAGCGCCCCACCTTGGGCTTCTGAGGGCATCATAGGGG
GACCCCTAGAGTCAGTTCACCACAGGCCCTGGGAGAGTCAAAGACCCCCGAGGGTGCCC
30 AGCCCCCACACTGTGACTCCTCACACTCAGCGATGACCTGTGGGGTGGGGGGCCCTGGG
ACGTTTTTTAAACCTAGGGTTTGGAGTCTGACTAAGCTCCATCCACGTCACACAGTT
TCTGTTTATATTTCTAGCTTTTTTTAATAAAATAAAAAAAAAAAGAAAACAGAAGTTTC
ACAACCCAGGGGCTGGCACGCCGTCTGTGCTGCCCGCCCCGCCCTGGCCCACCGGCC
CCACTCCCTGGGCACAGAGTCACACCCACTCATCCTCCGCCAACAGTCCAGGTACACA
35 GCAGCAGTCACTGTAACAGACTGCCACATACACACTCGGTCTCACACTCACCTGTGGGTT
TTGGTTCCGTTCAATTTGGGTTTTTAACCTTACAGGGTCAGTTCGCTTCACCTCCTTTT
GTATGGAGTTCCATCCGGGGGGTTTACCCCCCTGCTCCAGTCCTGAGGCCTCCTGACCCCT
GACGTTGTGATACGCCCCACAGAGATCTATGTTTCTTATATTATTATTGATAATAAT
TATTATAATATTATTATGTAATAAATTTATAAGAAATGAA
40

SEQ ID NO:2

45 CPP Amino Acid Sequence (Artificial/Synthetic)
RRSRTARAGRPGRNSSRPSAPR

SEQ ID NO:1079

target region within the 3'UTR of SHANK3
TTTTGGTTCCGTTCAATTTGGGTTTTTAACCTTACAGGGTCAGTTCGCTTCACCTCC
TTTTGTATGGAGTTCCAT
50

**Table 1: Exemplary ASO or AR Sequences Targeting
SHANK3 mRNA 3' UTR**

SEQ ID NO	Sequence	Name	ASO type
3	GTAAAGTTAAAAACCCAAATTGAAC	SHANK3 H22A(+1689+1713)	25mer
4	TTAAAGTTAAAAACCCAAATTGAAC	SHANK3 H22A(+1689+1713) 1mm_1	25mer
5	GTAAAGTTAAAAATCCAAATTGAAC	SHANK3 H22A(+1689+1713) 1mm_14	25mer
6	GTAAAGTTAAAAACTCAAATTGAAC	SHANK3 H22A(+1689+1713) 1mm_15	25mer
7	GTAAAGTTAAAAACCTAAATTGAAC	SHANK3 H22A(+1689+1713) 1mm_16	25mer
8	GTAAAGTTAAAAACCCAAATTGAAC	SHANK3 H22A(+1689+1713) 1mm_22	25mer
9	GTAAAGTTAAAAACCCAAATTGAAT	SHANK3 H22A(+1689+1713) 1mm_25	25mer
10	GTAAATTTAAAAACCCAAATTGAAC	SHANK3 H22A(+1689+1713) 1mm_6	25mer
11	ATAAAATTTAAAAACCCAAATTGAAC	SHANK3 H22A(+1689+1713) 2mm_1_6	25mer
12	GTAAAGTTAAAAACCCAAATTAAAC	SHANK3 H22A(+1689+1713) mm1	25mer
13	GTAAATTTAAAAACCCAAATTAAAC	SHANK3 H22A(+1689+1713) mm2	25mer
14	TGTAAAGTTAAAAATCCAAATTGAA	SHANK3 H22A(+1690+1714) 1mm_15	25mer
15	TGTAAAGTTAAAAACTCAAATTGAA	SHANK3 H22A(+1690+1714) 1mm_16	25mer
16	TGTAAAGTTAAAAACCTAAATTGAA	SHANK3 H22A(+1690+1714) 1mm_17	25mer
17	TTTAAAGTTAAAAACCCAAATTGAA	SHANK3 H22A(+1690+1714) 1mm_2	25mer
18	TGTAAAGTTAAAAACCCAAATTGAA	SHANK3 H22A(+1690+1714) 1mm_23	25mer
19	TGTAAATTTAAAAACCCAAATTGAA	SHANK3 H22A(+1690+1714) 1mm_7	25mer
20	TGTAAAGTTAAAAACCCAAATTAAA	SHANK3 H22A(+1690+1714) mm1	25mer
21	TGTAAATTTAAAAACCCAAATTAAA	SHANK3 H22A(+1690+1714) mm2	25mer
22	CTGTAAAGTTAAAAACCCAAATTGA	SHANK3 H22A(+1691+1715)	25mer
23	TTGTAAAGTTAAAAACCCAAATTGA	SHANK3 H22A(+1691+1715) 1mm_1	25mer
24	CTGTAAAGTTAAAAATCCAAATTGA	SHANK3 H22A(+1691+1715) 1mm_16	25mer
25	CTGTAAAGTTAAAAACTCAAATTGA	SHANK3 H22A(+1691+1715) 1mm_17	25mer
26	CTGTAAAGTTAAAAACCTAAATTGA	SHANK3 H22A(+1691+1715) 1mm_18	25mer
27	CTGTAAAGTTAAAAACCCAAATTGA	SHANK3 H22A(+1691+1715) 1mm_24	25mer
28	CTTTAAAGTTAAAAACCCAAATTGA	SHANK3 H22A(+1691+1715) 1mm_3	25mer
29	CTGTAAATTTAAAAACCCAAATTGA	SHANK3 H22A(+1691+1715) 1mm_8	25mer
30	CTGTAAAGTTAAAAACCCAAATTAA	SHANK3 H22A(+1691+1715) mm1	25mer
31	CTGTAAATTTAAAAACCCAAATTAA	SHANK3 H22A(+1691+1715) mm2	25mer
32	TCTGTAAAGTTAAAAACCCAAATTG	SHANK3 H22A(+1692+1716) 1mm_1	25mer
33	CCTGTAAAGTTAAAAATCCAAATTG	SHANK3 H22A(+1692+1716) 1mm_17	25mer
34	CCTGTAAAGTTAAAAACTCAAATTG	SHANK3 H22A(+1692+1716) 1mm_18	25mer
35	CCTGTAAAGTTAAAAACCTAAATTG	SHANK3 H22A(+1692+1716) 1mm_19	25mer
36	CTTGTAAAGTTAAAAACCCAAATTG	SHANK3 H22A(+1692+1716) 1mm_2	25mer
37	CCTTTAAAGTTAAAAACCCAAATTG	SHANK3 H22A(+1692+1716) 1mm_4	25mer
38	CCTGTAAATTTAAAAACCCAAATTG	SHANK3 H22A(+1692+1716) 1mm_9	25mer
39	CCTGTAAAGTTAAAAACCCAAATTA	SHANK3 H22A(+1692+1716) mm1	25mer

40	CCTGTAAAATTAAAAACCCAAATTA	SHANK3 H22A(+1692+1716) mm2	25mer
41	TCCTGTAAAGTTAAAAACCCAAATT	SHANK3 H22A(+1693+1717) 1mm_1	25mer
42	CCCTGTAAATTTAAAAACCCAAATT	SHANK3 H22A(+1693+1717) 1mm_10	25mer
43	CCCTGTAAAGTTAAAAATCCAAATT	SHANK3 H22A(+1693+1717) 1mm_18	25mer
44	CCCTGTAAAGTTAAAAACTCAAATT	SHANK3 H22A(+1693+1717) 1mm_19	25mer
45	CTCTGTAAAGTTAAAAACCCAAATT	SHANK3 H22A(+1693+1717) 1mm_2	25mer
46	CCCTGTAAAGTTAAAAACCTAAATT	SHANK3 H22A(+1693+1717) 1mm_20	25mer
47	CCTTGTAAAGTTAAAAACCCAAATT	SHANK3 H22A(+1693+1717) 1mm_3	25mer
48	CCCTTTAAAGTTAAAAACCCAAATT	SHANK3 H22A(+1693+1717) 1mm_5	25mer
49	CCCTGTAAAATTAAAAACCCAAATT	SHANK3 H22A(+1693+1717) mm1	25mer
50	CCCTATAAAATTAAAAACCCAAATT	SHANK3 H22A(+1693+1717) mm2	25mer
51	ACCCTGTAAAGTTAAAAACCCAAAT	SHANK3 H22A(+1694+1718)	25mer
52	ACCCTGTAAATTTAAAAACCCAAAT	SHANK3 H22A(+1694+1718) 1mm_11	25mer
53	ACCCTGTAAAGTTAAAAATCCAAAT	SHANK3 H22A(+1694+1718) 1mm_19	25mer
54	ATCCTGTAAAGTTAAAAACCCAAAT	SHANK3 H22A(+1694+1718) 1mm_2	25mer
55	ACCCTGTAAAGTTAAAAACTCAAAT	SHANK3 H22A(+1694+1718) 1mm_20	25mer
56	ACCCTGTAAAGTTAAAAACCTAAAT	SHANK3 H22A(+1694+1718) 1mm_21	25mer
57	ACTCTGTAAAGTTAAAAACCCAAAT	SHANK3 H22A(+1694+1718) 1mm_3	25mer
58	ACCTTGTAAAGTTAAAAACCCAAAT	SHANK3 H22A(+1694+1718) 1mm_4	25mer
59	ACCCTTTAAAGTTAAAAACCCAAAT	SHANK3 H22A(+1694+1718) 1mm_6	25mer
60	ACCCTGTAAAATTAAAAACCCAAAT	SHANK3 H22A(+1694+1718) mm1	25mer
61	ACCCTATAAAATTAAAAACCCAAAT	SHANK3 H22A(+1694+1718) mm2	25mer
62	GACCCTGTAAAGTTAAAAACCCAAA	SHANK3 H22A(+1695+1719)	25mer
63	TACCCTGTAAAGTTAAAAACCCAAA	SHANK3 H22A(+1695+1719) 1mm_1	25mer
64	GACCCTGTAAATTTAAAAACCCAAA	SHANK3 H22A(+1695+1719) 1mm_12	25mer
65	GACCCTGTAAAGTTAAAAATCCAAA	SHANK3 H22A(+1695+1719) 1mm_20	25mer
66	GACCCTGTAAAGTTAAAAACTCAA	SHANK3 H22A(+1695+1719) 1mm_21	25mer
67	GACCCTGTAAAGTTAAAAACCTAAA	SHANK3 H22A(+1695+1719) 1mm_22	25mer
68	GATCCTGTAAAGTTAAAAACCCAAA	SHANK3 H22A(+1695+1719) 1mm_3	25mer
69	GACTCTGTAAAGTTAAAAACCCAAA	SHANK3 H22A(+1695+1719) 1mm_4	25mer
70	GACCTTGTAAAGTTAAAAACCCAAA	SHANK3 H22A(+1695+1719) 1mm_5	25mer
71	GACCCTTTAAAGTTAAAAACCCAAA	SHANK3 H22A(+1695+1719) 1mm_7	25mer
72	GACCCTGTAAAATTAAAAACCCAAA	SHANK3 H22A(+1695+1719) mm1	25mer
73	GACCCTATAAAATTAAAAACCCAAA	SHANK3 H22A(+1695+1719) mm2	25mer
74	TGACCCTGTAAATTTAAAAACCCAA	SHANK3 H22A(+1696+1720) 1mm_13	25mer
75	TTACCCTGTAAAGTTAAAAACCCAA	SHANK3 H22A(+1696+1720) 1mm_2	25mer
76	TGACCCTGTAAAGTTAAAAATCCAA	SHANK3 H22A(+1696+1720) 1mm_21	25mer
77	TGACCCTGTAAAGTTAAAAACTCAA	SHANK3 H22A(+1696+1720) 1mm_22	25mer
78	TGACCCTGTAAAGTTAAAAACCTAA	SHANK3 H22A(+1696+1720) 1mm_23	25mer
79	TGATCCTGTAAAGTTAAAAACCCAA	SHANK3 H22A(+1696+1720) 1mm_4	25mer
80	TGACTCTGTAAAGTTAAAAACCCAA	SHANK3 H22A(+1696+1720) 1mm_5	25mer

81	TGACCTTGTAAGTTAAAAACCCAA	SHANK3 H22A(+1696+1720) 1mm_6	25mer
82	TGACCCTTTAAAGTTAAAAACCCAA	SHANK3 H22A(+1696+1720) 1mm_8	25mer
83	TAACCCTGTAAAATTAAAAACCCAA	SHANK3 H22A(+1696+1720) 2mm_2_13	25mer
84	TGACCCTGTAAAATTAAAAACCCAA	SHANK3 H22A(+1696+1720) mm1	25mer
85	TGACCCTATAAAATTAAAAACCCAA	SHANK3 H22A(+1696+1720) mm2	25mer
86	CTGACCCTGTAAAGTTAAAAACCCA	SHANK3 H22A(+1697+1721)	25mer
87	TTGACCCTGTAAAGTTAAAAACCCA	SHANK3 H22A(+1697+1721) 1mm_1	25mer
88	CTGACCCTGTAAATTTAAAAACCCA	SHANK3 H22A(+1697+1721) 1mm_14	25mer
89	CTGACCCTGTAAAGTTAAAAATCCA	SHANK3 H22A(+1697+1721) 1mm_22	25mer
90	CTGACCCTGTAAAGTTAAAAACTCA	SHANK3 H22A(+1697+1721) 1mm_23	25mer
91	CTGACCCTGTAAAGTTAAAAACCTA	SHANK3 H22A(+1697+1721) 1mm_24	25mer
92	CTTACCCTGTAAAGTTAAAAACCCA	SHANK3 H22A(+1697+1721) 1mm_3	25mer
93	CTGATCCTGTAAAGTTAAAAACCCA	SHANK3 H22A(+1697+1721) 1mm_5	25mer
94	CTGACTCTGTAAAGTTAAAAACCCA	SHANK3 H22A(+1697+1721) 1mm_6	25mer
95	CTGACCTTGTAAGTTAAAAACCCA	SHANK3 H22A(+1697+1721) 1mm_7	25mer
96	CTGACCCTTTAAAGTTAAAAACCCA	SHANK3 H22A(+1697+1721) 1mm_9	25mer
97	CTAACCCTGTAAAATTAAAAACCCA	SHANK3 H22A(+1697+1721) 2mm_3_14	25mer
98	CTGACCCTGTAAAATTAAAAACCCA	SHANK3 H22A(+1697+1721) mm1	25mer
99	CTGACCCTATAAAATTAAAAACCCA	SHANK3 H22A(+1697+1721) mm2	25mer
100	ACTGACCCTGTAAAGTTAAAAACCC	SHANK3 H22A(+1698+1722)	25mer
101	ACTGACCCTTTAAAGTTAAAAACCC	SHANK3 H22A(+1698+1722) 1mm_10	25mer
102	ACTGACCCTGTAAATTTAAAAACCC	SHANK3 H22A(+1698+1722) 1mm_15	25mer
103	ATTGACCCTGTAAAGTTAAAAACCC	SHANK3 H22A(+1698+1722) 1mm_2	25mer
104	ACTGACCCTGTAAAGTTAAAAATCC	SHANK3 H22A(+1698+1722) 1mm_23	25mer
105	ACTGACCCTGTAAAGTTAAAAACTC	SHANK3 H22A(+1698+1722) 1mm_24	25mer
106	ACTGACCCTGTAAAGTTAAAAACCT	SHANK3 H22A(+1698+1722) 1mm_25	25mer
107	ACTTACCCTGTAAAGTTAAAAACCC	SHANK3 H22A(+1698+1722) 1mm_4	25mer
108	ACTGATCCTGTAAAGTTAAAAACCC	SHANK3 H22A(+1698+1722) 1mm_6	25mer
109	ACTGACTCTGTAAAGTTAAAAACCC	SHANK3 H22A(+1698+1722) 1mm_7	25mer
110	ACTGACCTTGTAAGTTAAAAACCC	SHANK3 H22A(+1698+1722) 1mm_8	25mer
111	ACTAACCCTGTAAAATTAAAAACCC	SHANK3 H22A(+1698+1722) 2mm_4_15	25mer
112	ACTGACCCTGTAAAATTAAAAACCC	SHANK3 H22A(+1698+1722) mm1	25mer
113	ACTGACCCTATAAAATTAAAAACCC	SHANK3 H22A(+1698+1722) mm2	25mer
114	AACTGACCCTTTAAAGTTAAAAACC	SHANK3 H22A(+1699+1723) 1mm_11	25mer
115	AACTGACCCTGTAAATTTAAAAACC	SHANK3 H22A(+1699+1723) 1mm_16	25mer
116	AACTGACCCTGTAAAGTTAAAAATC	SHANK3 H22A(+1699+1723) 1mm_24	25mer
117	AACTGACCCTGTAAAGTTAAAAACT	SHANK3 H22A(+1699+1723) 1mm_25	25mer
118	AATTGACCCTGTAAAGTTAAAAACC	SHANK3 H22A(+1699+1723) 1mm_3	25mer
119	AACTTACCCTGTAAAGTTAAAAACC	SHANK3 H22A(+1699+1723) 1mm_5	25mer

120	AACTGATCCTGTAAAGTTAAAAACC	SHANK3 H22A(+1699+1723) 1mm_7	25mer
121	AACTGACTCTGTAAAGTTAAAAACC	SHANK3 H22A(+1699+1723) 1mm_8	25mer
122	AACTGACCTTGTAAAGTTAAAAACC	SHANK3 H22A(+1699+1723) 1mm_9	25mer
123	AACTAACCCCTGTAAAATTTAAAAACC	SHANK3 H22A(+1699+1723) 2mm_5_16	25mer
124	AACTGACCCTGTAAAATTTAAAAACC	SHANK3 H22A(+1699+1723) mm1	25mer
125	AACTGACCCTATAAAAATTTAAAAACC	SHANK3 H22A(+1699+1723) mm2	25mer
126	GAACTGACCCTGTAAAGTTAAAAAC	SHANK3 H22A(+1700+1724)	25mer
127	TAACTGACCCTGTAAAGTTAAAAAC	SHANK3 H22A(+1700+1724) 1mm_1	25mer
128	GAACTGACCTTGTAAAGTTAAAAAC	SHANK3 H22A(+1700+1724) 1mm_10	25mer
129	GAACTGACCCTTTTAAAGTTAAAAAC	SHANK3 H22A(+1700+1724) 1mm_12	25mer
130	GAACTGACCCTGTAAATTTAAAAAC	SHANK3 H22A(+1700+1724) 1mm_17	25mer
131	GAACTGACCCTGTAAAGTTAAAAAT	SHANK3 H22A(+1700+1724) 1mm_25	25mer
132	GAATTGACCCTGTAAAGTTAAAAAC	SHANK3 H22A(+1700+1724) 1mm_4	25mer
133	GAACTTACCCTGTAAAGTTAAAAAC	SHANK3 H22A(+1700+1724) 1mm_6	25mer
134	GAACTGATCCTGTAAAGTTAAAAAC	SHANK3 H22A(+1700+1724) 1mm_8	25mer
135	GAACTGACTCTGTAAAGTTAAAAAC	SHANK3 H22A(+1700+1724) 1mm_9	25mer
136	AAACTGACCCTATAAAGTTAAAAAC	SHANK3 H22A(+1700+1724) 2mm_1_12	25mer
137	AAACTGACCCTGTAAAATTTAAAAAC	SHANK3 H22A(+1700+1724) 2mm_1_17	25mer
138	AAACTAACCCCTGTAAAGTTAAAAAC	SHANK3 H22A(+1700+1724) 2mm_1_6	25mer
139	GAACTAACCCCTGTAAAATTTAAAAAC	SHANK3 H22A(+1700+1724) 2mm_6_17	25mer
140	GAACTGACCCTGTAAAATTTAAAAAC	SHANK3 H22A(+1700+1724) mm1	25mer
141	GAACTGACCCTATAAAAATTTAAAAAC	SHANK3 H22A(+1700+1724) mm2	25mer
142	GGAAGTACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1725)	25mer
143	TGAAGTACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 1mm_1	25mer
144	GGAAGTACTCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 1mm_10	25mer
145	GGAAGTACCTTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 1mm_11	25mer
146	GGAAGTACCCTTTTAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 1mm_13	25mer
147	GGAAGTACCCTGTAAATTTAAAAA	SHANK3 H22A(+1701+1725) 1mm_18	25mer
148	GTAAGTACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 1mm_2	25mer
149	GGAATTGACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 1mm_5	25mer
150	GGAAGTACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 1mm_7	25mer
151	GGAAGTGATCCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 1mm_9	25mer
152	AGAAGTACCCTATAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 2mm_1_13	25mer
153	AGAAGTACCCTGTAAAATTTAAAAA	SHANK3 H22A(+1701+1725) 2mm_1_18	25mer
154	AAAAGTACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 2mm_1_2	25mer
155	AGAAGTACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 2mm_1_7	25mer

156	GAAACTGACCCTATAAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 2mm_2_13	25mer
157	GAAACTGACCCTGTAAAATTAAAAA	SHANK3 H22A(+1701+1725) 2mm_2_18	25mer
158	GAAACTAACCCCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1725) 2mm_2_7	25mer
159	GGAACTAACCCCTGTAAAATTAAAAA	SHANK3 H22A(+1701+1725) 2mm_7_18	25mer
160	GGAACTGACCCTGTAAAATTAAAAA	SHANK3 H22A(+1701+1725) mm1	25mer
161	GGAACTGACCCTATAAAATTAAAAA	SHANK3 H22A(+1701+1725) mm2	25mer
162	TGGAAGTACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 1mm_1	25mer
163	CGGAAGTGATCCTGTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 1mm_10	25mer
164	CGGAAGTGACTCTGTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 1mm_11	25mer
165	CGGAAGTGACCTTGTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 1mm_12	25mer
166	CGGAAGTGACCCTTTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 1mm_14	25mer
167	CGGAAGTGACCCTGTAAATTTAAAAA	SHANK3 H22A(+1702+1726) 1mm_19	25mer
168	CTGAAGTGACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 1mm_2	25mer
169	CGTAAGTGACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 1mm_3	25mer
170	CGGAATTGACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 1mm_6	25mer
171	CGGAAGTTACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 1mm_8	25mer
172	CAGAAGTGACCCTATAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 2mm_2_14	25mer
173	CAGAAGTGACCCTGTAAAATTAAAAA	SHANK3 H22A(+1702+1726) 2mm_2_19	25mer
174	CAAAAGTGACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 2mm_2_3	25mer
175	CAGAAGTAACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 2mm_2_8	25mer
176	CGAAAGTGACCCTATAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 2mm_3_14	25mer
177	CGAAAGTGACCCTGTAAAATTAAAAA	SHANK3 H22A(+1702+1726) 2mm_3_19	25mer
178	CGAAAGTAACCCTGTAAAGTTAAAAA	SHANK3 H22A(+1702+1726) 2mm_3_8	25mer
179	CGGAAGTAACCCTGTAAAATTAAAAA	SHANK3 H22A(+1702+1726) 2mm_8_19	25mer
180	CGGAAGTGACCCTGTAAAATTAAAAA	SHANK3 H22A(+1702+1726) mm1	25mer
181	CGGAAGTGACCCTATAAAATTAAAAA	SHANK3 H22A(+1702+1726) mm2	25mer
182	GCGGAAGTGACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727)	25mer
183	TCGGAAGTGACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 1mm_1	25mer
184	GCGGAAGTGATCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 1mm_11	25mer
185	GCGGAAGTGACTCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 1mm_12	25mer
186	GCGGAAGTGACCTTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 1mm_13	25mer
187	GCGGAAGTGACCCTTTAAAGTTAAA	SHANK3 H22A(+1703+1727) 1mm_15	25mer
188	GTGGAAGTGACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 1mm_2	25mer
189	GCGGAAGTGACCCTGTAAATTTAAA	SHANK3 H22A(+1703+1727) 1mm_20	25mer
190	GCTGAAGTGACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 1mm_3	25mer
191	GCGTAAGTGACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 1mm_4	25mer

192	GCGGAATTGACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 1mm_7	25mer
193	GCGGAACCTTACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 1mm_9	25mer
194	ACGGAAGTACCCTATAAAGTTAAA	SHANK3 H22A(+1703+1727) 2mm_1_15	25mer
195	ACGGAAGTACCCTGTAAATTTAAA	SHANK3 H22A(+1703+1727) 2mm_1_20	25mer
196	ACAGAACTGACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 2mm_1_3	25mer
197	ACGAAACTGACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 2mm_1_4	25mer
198	ACGGAAGTACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 2mm_1_9	25mer
199	GCAGAACTGACCCTATAAAGTTAAA	SHANK3 H22A(+1703+1727) 2mm_3_15	25mer
200	GCAGAACTGACCCTGTAAATTTAAA	SHANK3 H22A(+1703+1727) 2mm_3_20	25mer
201	GCAAAACTGACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 2mm_3_4	25mer
202	GCAGAACTAACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 2mm_3_9	25mer
203	GCGAAACTGACCCTATAAAGTTAAA	SHANK3 H22A(+1703+1727) 2mm_4_15	25mer
204	GCGAAACTGACCCTGTAAATTTAAA	SHANK3 H22A(+1703+1727) 2mm_4_20	25mer
205	GCGAAAGTACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1727) 2mm_4_9	25mer
206	GCGGAAGTACCCTGTAAATTTAAA	SHANK3 H22A(+1703+1727) 2mm_9_20	25mer
207	GCGGAAGTACCCTGTAAATTTAAA	SHANK3 H22A(+1703+1727) mm1	25mer
208	GCGGAAGTACCCTATAAATTTAAA	SHANK3 H22A(+1703+1727) mm2	25mer
209	AGCGGAAGTACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728)	25mer
210	AGCGGAAGTACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 1mm_10	25mer
211	AGCGGAAGTGATCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 1mm_12	25mer
212	AGCGGAAGTGACTCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 1mm_13	25mer
213	AGCGGAAGTGACCTTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 1mm_14	25mer
214	AGCGGAAGTGACCTTTAAAGTTAA	SHANK3 H22A(+1704+1728) 1mm_16	25mer
215	ATCGGAAGTACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 1mm_2	25mer
216	AGCGGAAGTACCCTGTAAATTTAA	SHANK3 H22A(+1704+1728) 1mm_21	25mer
217	AGTGGAAGTACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 1mm_3	25mer
218	AGCTGAAGTACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 1mm_4	25mer
219	AGCGTAAGTACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 1mm_5	25mer
220	AGCGGAATTGACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 1mm_8	25mer
221	AGCGGAAGTACCCTGTAAATTTAA	SHANK3 H22A(+1704+1728) 2mm_10_21	25mer
222	AACGGAAGTACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 2mm_2_10	25mer
223	AACGGAAGTACCCTATAAAGTTAA	SHANK3 H22A(+1704+1728) 2mm_2_16	25mer
224	AACGGAAGTACCCTGTAAATTTAA	SHANK3 H22A(+1704+1728) 2mm_2_21	25mer
225	AACAGAACTGACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 2mm_2_4	25mer

226	AACGAACTGACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 2mm_2_5	25mer
227	AGCAGAACTAACCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 2mm_4_10	25mer
228	AGCAGAACTGACCCTATAAAGTTAA	SHANK3 H22A(+1704+1728) 2mm_4_16	25mer
229	AGCAGAACTGACCCTGTAAAATTAA	SHANK3 H22A(+1704+1728) 2mm_4_21	25mer
230	AGCAAACTGACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 2mm_4_5	25mer
231	AGCGAACTAACCTGTAAAGTTAA	SHANK3 H22A(+1704+1728) 2mm_5_10	25mer
232	AGCGAACTGACCCTATAAAGTTAA	SHANK3 H22A(+1704+1728) 2mm_5_16	25mer
233	AGCGAACTGACCCTGTAAAATTAA	SHANK3 H22A(+1704+1728) 2mm_5_21	25mer
234	AGCGGAACTGACCCTGTAAAATTAA	SHANK3 H22A(+1704+1728) mm1	25mer
235	AGCGGAACTGACCCTATAAAATTAA	SHANK3 H22A(+1704+1728) mm2	25mer
236	AAGCGGAACTTACCCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 1mm_11	25mer
237	AAGCGGAACTGATCCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 1mm_13	25mer
238	AAGCGGAACTGACTCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 1mm_14	25mer
239	AAGCGGAACTGACCTTGTAAAGTTA	SHANK3 H22A(+1705+1729) 1mm_15	25mer
240	AAGCGGAACTGACCCTTTAAAGTTA	SHANK3 H22A(+1705+1729) 1mm_17	25mer
241	AAGCGGAACTGACCCTGTAAATTTA	SHANK3 H22A(+1705+1729) 1mm_22	25mer
242	AATCGGAACTGACCCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 1mm_3	25mer
243	AAGTGGAAGTACCCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 1mm_4	25mer
244	AAGCTGAAGTACCCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 1mm_5	25mer
245	AAGCGTAAGTACCCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 1mm_6	25mer
246	AAGCGGAATTGACCCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 1mm_9	25mer
247	AAGCGGAACTAACCTGTAAAATTA	SHANK3 H22A(+1705+1729) 2mm_11_22	25mer
248	AAACGGAACTAACCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 2mm_3_11	25mer
249	AAACGGAACTGACCCTATAAAGTTA	SHANK3 H22A(+1705+1729) 2mm_3_17	25mer
250	AAACGGAACTGACCCTGTAAAATTA	SHANK3 H22A(+1705+1729) 2mm_3_22	25mer
251	AAACAGAACTGACCCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 2mm_3_5	25mer
252	AAACGAACTGACCCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 2mm_3_6	25mer
253	AAGCAGAACTAACCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 2mm_5_11	25mer
254	AAGCAGAACTGACCCTATAAAGTTA	SHANK3 H22A(+1705+1729) 2mm_5_17	25mer
255	AAGCAGAACTGACCCTGTAAAATTA	SHANK3 H22A(+1705+1729) 2mm_5_22	25mer
256	AAGCAAACTGACCCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 2mm_5_6	25mer
257	AAGCGAACTAACCTGTAAAGTTA	SHANK3 H22A(+1705+1729) 2mm_6_11	25mer

258	AAGCGAACTGACCCTATAAAAGTTA	SHANK3 H22A(+1705+1729) 2mm_6_17	25mer
259	AAGCGAACTGACCCTGTAAAATTA	SHANK3 H22A(+1705+1729) 2mm_6_22	25mer
260	AAGCGGAACTGACCCTGTAAAATTA	SHANK3 H22A(+1705+1729) mm1	25mer
261	AAGCGGAACTGACCCTATAAAATTA	SHANK3 H22A(+1705+1729) mm2	25mer
262	GAAGCGGAACTGACCCTGTAAAGTT	SHANK3 H22A(+1706+1730)	25mer
263	TAAGCGGAACTGACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 1mm_1	25mer
264	GAAGCGGAATTGACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 1mm_10	25mer
265	GAAGCGGAACTTACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 1mm_12	25mer
266	GAAGCGGAACTGATCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 1mm_14	25mer
267	GAAGCGGAACTGACTCTGTAAAGTT	SHANK3 H22A(+1706+1730) 1mm_15	25mer
268	GAAGCGGAACTGACCTTGTAAAGTT	SHANK3 H22A(+1706+1730) 1mm_16	25mer
269	GAAGCGGAACTGACCCTTTAAAGTT	SHANK3 H22A(+1706+1730) 1mm_18	25mer
270	GAAGCGGAACTGACCCTGTAAATTT	SHANK3 H22A(+1706+1730) 1mm_23	25mer
271	GAATCGGAACTGACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 1mm_4	25mer
272	GAAGTGGAAGTACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 1mm_5	25mer
273	GAAGCTGAAGTACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 1mm_6	25mer
274	GAAGCGTAACTGACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 1mm_7	25mer
275	AAAGCGGAACTAACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 2mm_1_12	25mer
276	AAAGCGGAACTGACCCTATAAAAGTT	SHANK3 H22A(+1706+1730) 2mm_1_18	25mer
277	AAAGCGGAACTGACCCTGTAAAATT	SHANK3 H22A(+1706+1730) 2mm_1_23	25mer
278	AAAACGGAAGTACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 2mm_1_4	25mer
279	AAAGCAGAACTGACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 2mm_1_6	25mer
280	AAAGCGAACTGACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 2mm_1_7	25mer
281	GAAGCGGAACTAACCCTGTAAAATT	SHANK3 H22A(+1706+1730) 2mm_12_23	25mer
282	GAAACGGAAGTACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 2mm_4_12	25mer
283	GAAACGGAAGTACCCTATAAAAGTT	SHANK3 H22A(+1706+1730) 2mm_4_18	25mer
284	GAAACGGAAGTACCCTGTAAAATT	SHANK3 H22A(+1706+1730) 2mm_4_23	25mer
285	GAAACAGAACTGACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 2mm_4_6	25mer
286	GAAACGAACTGACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 2mm_4_7	25mer
287	GAAGCAGAACTAACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 2mm_6_12	25mer
288	GAAGCAGAACTGACCCTATAAAAGTT	SHANK3 H22A(+1706+1730) 2mm_6_18	25mer
289	GAAGCAGAACTGACCCTGTAAAATT	SHANK3 H22A(+1706+1730) 2mm_6_23	25mer
290	GAAGCAAACTGACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 2mm_6_7	25mer

291	GAAGCGAACTAACCCTGTAAAGTT	SHANK3 H22A(+1706+1730) 2mm_7_12	25mer
292	GAAGCGAACTGACCCTATAAAGTT	SHANK3 H22A(+1706+1730) 2mm_7_18	25mer
293	GAAGCGAACTGACCCTGTAAAATT	SHANK3 H22A(+1706+1730) 2mm_7_23	25mer
294	GAAGCGGAACTGACCCTGTAAAATT	SHANK3 H22A(+1706+1730) mm1	25mer
295	GAAGCGGAACTGACCCTATAAAAATT	SHANK3 H22A(+1706+1730) mm2	25mer
296	TGAAGCGGAATTGACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 1mm_11	25mer
297	TGAAGCGGAATTACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 1mm_13	25mer
298	TGAAGCGGAACTGATCCTGTAAAGT	SHANK3 H22A(+1707+1731) 1mm_15	25mer
299	TGAAGCGGAACTGACTCTGTAAAGT	SHANK3 H22A(+1707+1731) 1mm_16	25mer
300	TGAAGCGGAACTGACCTTGTAAAGT	SHANK3 H22A(+1707+1731) 1mm_17	25mer
301	TGAAGCGGAACTGACCCTTTAAAGT	SHANK3 H22A(+1707+1731) 1mm_19	25mer
302	TTAAGCGGAACTGACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 1mm_2	25mer
303	TGAAGCGGAACTGACCCTGTAAATT	SHANK3 H22A(+1707+1731) 1mm_24	25mer
304	TGAATCGGAACTGACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 1mm_5	25mer
305	TGAAGTGGAAGTACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 1mm_6	25mer
306	TGAAGCTGAAGTACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 1mm_7	25mer
307	TGAAGCGTAACTGACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 1mm_8	25mer
308	TGAAGCGGAACTAACCCTGTAAAT	SHANK3 H22A(+1707+1731) 2mm_13_24	25mer
309	TAAAGCGGAACTAACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 2mm_2_13	25mer
310	TAAAGCGGAACTGACCCTATAAAGT	SHANK3 H22A(+1707+1731) 2mm_2_19	25mer
311	TAAAGCGGAACTGACCCTGTAAAT	SHANK3 H22A(+1707+1731) 2mm_2_24	25mer
312	TAAAACGGAACTGACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 2mm_2_5	25mer
313	TAAAGCAGAACTGACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 2mm_2_7	25mer
314	TAAAGCGAACTGACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 2mm_2_8	25mer
315	TGAAACGGAACTAACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 2mm_5_13	25mer
316	TGAAACGGAACTGACCCTATAAAGT	SHANK3 H22A(+1707+1731) 2mm_5_19	25mer
317	TGAAACGGAACTGACCCTGTAAAT	SHANK3 H22A(+1707+1731) 2mm_5_24	25mer
318	TGAAACAGAACTGACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 2mm_5_7	25mer
319	TGAAACGAACTGACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 2mm_5_8	25mer
320	TGAAGCAGAACTAACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 2mm_7_13	25mer
321	TGAAGCAGAACTGACCCTATAAAGT	SHANK3 H22A(+1707+1731) 2mm_7_19	25mer
322	TGAAGCAGAACTGACCCTGTAAAT	SHANK3 H22A(+1707+1731) 2mm_7_24	25mer

323	TGAAGCAAACTGACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 2mm_7_8	25mer
324	TGAAGCGAACTAACCCTGTAAAGT	SHANK3 H22A(+1707+1731) 2mm_8_13	25mer
325	TGAAGCGAACTGACCCTATAAAGT	SHANK3 H22A(+1707+1731) 2mm_8_19	25mer
326	TGAAGCGAACTGACCCTGTAAAAT	SHANK3 H22A(+1707+1731) 2mm_8_24	25mer
327	TGAAGCGGAACTGACCCTGTAAAAT	SHANK3 H22A(+1707+1731) mm1	25mer
328	TGAAGCGGAACTGACCCTATAAAAT	SHANK3 H22A(+1707+1731) mm2	25mer
329	TTGAAGCGGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 1mm_1	25mer
330	GTGAAGCGGAATTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 1mm_12	25mer
331	GTGAAGCGGAACTTACCCTGTAAAG	SHANK3 H22A(+1708+1732) 1mm_14	25mer
332	GTGAAGCGGAACTGATCCTGTAAAG	SHANK3 H22A(+1708+1732) 1mm_16	25mer
333	GTGAAGCGGAACTGACTCTGTAAAG	SHANK3 H22A(+1708+1732) 1mm_17	25mer
334	GTGAAGCGGAACTGACCTTGTAAAG	SHANK3 H22A(+1708+1732) 1mm_18	25mer
335	GTGAAGCGGAACTGACCCTTTAAAG	SHANK3 H22A(+1708+1732) 1mm_20	25mer
336	GTGAAGCGGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 1mm_3	25mer
337	GTGAATCGGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 1mm_6	25mer
338	GTGAAGTGGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 1mm_7	25mer
339	GTGAAGCTGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 1mm_8	25mer
340	GTGAAGCGTAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 1mm_9	25mer
341	ATGAAGCGGAACTAACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_1_14	25mer
342	ATGAAGCGGAACTGACCCTATAAAG	SHANK3 H22A(+1708+1732) 2mm_1_20	25mer
343	ATGAAGCGGAACTGACCCTGTAAAA	SHANK3 H22A(+1708+1732) 2mm_1_25	25mer
344	ATAAAGCGGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_1_3	25mer
345	ATGAAACGGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_1_6	25mer
346	ATGAAGCAGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_1_8	25mer
347	ATGAAGCGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_1_9	25mer
348	GTGAAGCGGAACTAACCCTGTAAAA	SHANK3 H22A(+1708+1732) 2mm_14_25	25mer
349	GTAAAGCGGAACTAACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_3_14	25mer
350	GTAAAGCGGAACTGACCCTATAAAG	SHANK3 H22A(+1708+1732) 2mm_3_20	25mer
351	GTAAAGCGGAACTGACCCTGTAAAA	SHANK3 H22A(+1708+1732) 2mm_3_25	25mer
352	GTAAAACGGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_3_6	25mer
353	GTAAAGCAGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_3_8	25mer
354	GTAAAGCGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_3_9	25mer
355	GTGAAACGGAACTAACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_6_14	25mer

356	GTGAAACGGAAGTACCCTATAAAG	SHANK3 H22A(+1708+1732) 2mm_6_20	25mer
357	GTGAAACGGAAGTACCCTGTAAAA	SHANK3 H22A(+1708+1732) 2mm_6_25	25mer
358	GTGAAACAGAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_6_8	25mer
359	GTGAAACGAAAGTACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_6_9	25mer
360	GTGAAGCAGAACTAACCCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_8_14	25mer
361	GTGAAGCAGAACTGACCCTATAAAG	SHANK3 H22A(+1708+1732) 2mm_8_20	25mer
362	GTGAAGCAGAACTGACCCTGTAAAA	SHANK3 H22A(+1708+1732) 2mm_8_25	25mer
363	GTGAAGCAAACTGACCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_8_9	25mer
364	GTGAAGCGAACTAACCCCTGTAAAG	SHANK3 H22A(+1708+1732) 2mm_9_14	25mer
365	GTGAAGCGAACTGACCCTATAAAG	SHANK3 H22A(+1708+1732) 2mm_9_20	25mer
366	GTGAAGCGAACTGACCCTGTAAAA	SHANK3 H22A(+1708+1732) 2mm_9_25	25mer
367	GTGAAGCGGAAGTACCCTGTAAAA	SHANK3 H22A(+1708+1732) mm1	25mer
368	GTGAAGCGGAAGTACCCTATAAAA	SHANK3 H22A(+1708+1732) mm2	25mer
369	GGTGAAGCGGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733)	25mer
370	TGTGAAGCGGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733) 1mm_1	25mer
371	GGTGAAGCGTAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733) 1mm_10	25mer
372	GGTGAAGCGGAATTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 1mm_13	25mer
373	GGTGAAGCGGAATTACCCTGTAAA	SHANK3 H22A(+1709+1733) 1mm_15	25mer
374	GGTGAAGCGGAAGTATCCTGTAAA	SHANK3 H22A(+1709+1733) 1mm_17	25mer
375	GGTGAAGCGGAAGTACTCTGTAAA	SHANK3 H22A(+1709+1733) 1mm_18	25mer
376	GGTGAAGCGGAAGTACCTTGTAAA	SHANK3 H22A(+1709+1733) 1mm_19	25mer
377	GTTGAAGCGGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733) 1mm_2	25mer
378	GGTGAAGCGGAAGTACCCTTTAAA	SHANK3 H22A(+1709+1733) 1mm_21	25mer
379	GGTTAAGCGGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733) 1mm_4	25mer
380	GGTGAATCGGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733) 1mm_7	25mer
381	GGTGAAGTGGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733) 1mm_8	25mer
382	GGTGAAGCTGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733) 1mm_9	25mer
383	AGTGAAGCGAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_1_10	25mer
384	AGTGAAGCGGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_1_15	25mer
385	AATGAAGCGGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_1_2	25mer
386	AGTGAAGCGGAAGTACCCTATAAA	SHANK3 H22A(+1709+1733) 2mm_1_21	25mer
387	AGTAAAGCGGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_1_4	25mer
388	AGTGAACGGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_1_7	25mer
389	AGTGAAGCAGAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_1_9	25mer

390	GGTGAAGCGAACTAACCCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_10_15	25mer
391	GGTGAAGCGAACTGACCCTATAAA	SHANK3 H22A(+1709+1733) 2mm_10_21	25mer
392	GATGAAGCGAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_2_10	25mer
393	GATGAAGCGGAACTAACCCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_2_15	25mer
394	GATGAAGCGGAACTGACCCTATAAA	SHANK3 H22A(+1709+1733) 2mm_2_21	25mer
395	GATAAAGCGGAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_2_4	25mer
396	GATGAAACGGAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_2_7	25mer
397	GATGAAGCAGAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_2_9	25mer
398	GGTAAAGCGGAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_4_10	25mer
399	GGTAAAGCGGAACTAACCCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_4_15	25mer
400	GGTAAAGCGGAACTGACCCTATAAA	SHANK3 H22A(+1709+1733) 2mm_4_21	25mer
401	GGTAAAACGGAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_4_7	25mer
402	GGTAAAGCAGAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_4_9	25mer
403	GGTGAACGAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_7_10	25mer
404	GGTGAACGGAATAACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_7_15	25mer
405	GGTGAACGGAATAACCCTATAAA	SHANK3 H22A(+1709+1733) 2mm_7_21	25mer
406	GGTGAACAGAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_7_9	25mer
407	GGTGAAGCAAACTGACCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_9_10	25mer
408	GGTGAAGCAGAACTAACCCCTGTAAA	SHANK3 H22A(+1709+1733) 2mm_9_15	25mer
409	GGTGAAGCAGAACTGACCCTATAAA	SHANK3 H22A(+1709+1733) 2mm_9_21	25mer
410	GGTGAAGCGGAACTGACCCTATAAA	SHANK3 H22A(+1709+1733) mm1	25mer
411	AGGTGAAGCGGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734)	25mer
412	AGGTGAAGCTGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 1mm_10	25mer
413	AGGTGAAGCGTAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 1mm_11	25mer
414	AGGTGAAGCGGAATTGACCCTGTAA	SHANK3 H22A(+1710+1734) 1mm_14	25mer
415	AGGTGAAGCGGAACTTACCCTGTAA	SHANK3 H22A(+1710+1734) 1mm_16	25mer
416	AGGTGAAGCGGAACTGATCCTGTAA	SHANK3 H22A(+1710+1734) 1mm_18	25mer
417	AGGTGAAGCGGAACTGACTCTGTAA	SHANK3 H22A(+1710+1734) 1mm_19	25mer
418	ATGTGAAGCGGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 1mm_2	25mer
419	AGGTGAAGCGGAACTGACCTTGTAA	SHANK3 H22A(+1710+1734) 1mm_20	25mer
420	AGGTGAAGCGGAACTGACCCTTTAA	SHANK3 H22A(+1710+1734) 1mm_22	25mer
421	AGTTGAAGCGGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 1mm_3	25mer

422	AGGTTAAGCGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 1mm_5	25mer
423	AGGTGAATCGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 1mm_8	25mer
424	AGGTGAAGTGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 1mm_9	25mer
425	AGGTGAAGCAAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_10_11	25mer
426	AGGTGAAGCAGAACTAACCCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_10_16	25mer
427	AGGTGAAGCAGAACTGACCCTATAA	SHANK3 H22A(+1710+1734) 2mm_10_22	25mer
428	AGGTGAAGCGAACTAACCCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_11_16	25mer
429	AGGTGAAGCGAACTGACCCTATAA	SHANK3 H22A(+1710+1734) 2mm_11_22	25mer
430	AAGTGAAGCAGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_2_10	25mer
431	AAGTGAAGCGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_2_11	25mer
432	AAGTGAAGCGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_2_16	25mer
433	AAGTGAAGCGGAAGTACCCTATAA	SHANK3 H22A(+1710+1734) 2mm_2_22	25mer
434	AAATGAAGCGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_2_3	25mer
435	AAGTAAAGCGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_2_5	25mer
436	AAGTAAACGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_2_8	25mer
437	AGATGAAGCAGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_3_10	25mer
438	AGATGAAGCGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_3_11	25mer
439	AGATGAAGCGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_3_16	25mer
440	AGATGAAGCGGAAGTACCCTATAA	SHANK3 H22A(+1710+1734) 2mm_3_22	25mer
441	AGATAAAGCGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_3_5	25mer
442	AGATGAAACGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_3_8	25mer
443	AGGTAAAGCAGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_5_10	25mer
444	AGGTAAAGCGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_5_11	25mer
445	AGGTAAAGCGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_5_16	25mer
446	AGGTAAAGCGGAAGTACCCTATAA	SHANK3 H22A(+1710+1734) 2mm_5_22	25mer
447	AGGTAAACGGAAGTACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_5_8	25mer
448	AGGTGAAACAGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_8_10	25mer
449	AGGTGAAACGAACTGACCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_8_11	25mer

450	AGGTGAAACGGAACTAACCCCTGTAA	SHANK3 H22A(+1710+1734) 2mm_8_16	25mer
451	AGGTGAAACGGAACTGACCCTATAA	SHANK3 H22A(+1710+1734) 2mm_8_22	25mer
452	AGGTGAAGCGGAACTGACCCTATAA	SHANK3 H22A(+1710+1734) mm1	25mer
453	TAGGTGAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 1mm_1	25mer
454	GAGGTGAAGTGGAAGCTGACCCTGTA	SHANK3 H22A(+1711+1735) 1mm_10	25mer
455	GAGGTGAAGCTGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 1mm_11	25mer
456	GAGGTGAAGCGTAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 1mm_12	25mer
457	GAGGTGAAGCGGAATTGACCCTGTA	SHANK3 H22A(+1711+1735) 1mm_15	25mer
458	GAGGTGAAGCGGAACTTACCCTGTA	SHANK3 H22A(+1711+1735) 1mm_17	25mer
459	GAGGTGAAGCGGAACTGATCCTGTA	SHANK3 H22A(+1711+1735) 1mm_19	25mer
460	GAGGTGAAGCGGAACTGACTCTGTA	SHANK3 H22A(+1711+1735) 1mm_20	25mer
461	GAGGTGAAGCGGAACTGACCTTGTA	SHANK3 H22A(+1711+1735) 1mm_21	25mer
462	GAGGTGAAGCGGAACTGACCCTTTA	SHANK3 H22A(+1711+1735) 1mm_23	25mer
463	GATGTGAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 1mm_3	25mer
464	GAGTTGAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 1mm_4	25mer
465	GAGGTGAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 1mm_6	25mer
466	GAGGTGAATCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 1mm_9	25mer
467	AAGGTGAAGCAGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_1_11	25mer
468	AAGGTGAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_1_12	25mer
469	AAGGTGAAGCGGAACTAACCCCTGTA	SHANK3 H22A(+1711+1735) 2mm_1_17	25mer
470	AAGGTGAAGCGGAACTGACCCTATA	SHANK3 H22A(+1711+1735) 2mm_1_23	25mer
471	AAAGTGAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_1_3	25mer
472	AAGATGAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_1_4	25mer
473	AAGGTAAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_1_6	25mer
474	AAGGTGAAACGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_1_9	25mer
475	GAGGTGAAGCAAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_11_12	25mer
476	GAGGTGAAGCAGAACTAACCCCTGTA	SHANK3 H22A(+1711+1735) 2mm_11_17	25mer
477	GAGGTGAAGCAGAACTGACCCTATA	SHANK3 H22A(+1711+1735) 2mm_11_23	25mer
478	GAGGTGAAGCGGAACTAACCCCTGTA	SHANK3 H22A(+1711+1735) 2mm_12_17	25mer
479	GAGGTGAAGCGGAACTGACCCTATA	SHANK3 H22A(+1711+1735) 2mm_12_23	25mer
480	GAAGTGAAGCAGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_3_11	25mer
481	GAAGTGAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_3_12	25mer

482	GAAGTGAAGCGGAACTAACCCCTGTA	SHANK3 H22A(+1711+1735) 2mm_3_17	25mer
483	GAAGTGAAGCGGAACTGACCCTATA	SHANK3 H22A(+1711+1735) 2mm_3_23	25mer
484	GAAATGAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_3_4	25mer
485	GAAGTAAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_3_6	25mer
486	GAAGTGAAACGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_3_9	25mer
487	GAGATGAAGCAGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_4_11	25mer
488	GAGATGAAGCGAAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_4_12	25mer
489	GAGATGAAGCGGAACTAACCCCTGTA	SHANK3 H22A(+1711+1735) 2mm_4_17	25mer
490	GAGATGAAGCGGAACTGACCCTATA	SHANK3 H22A(+1711+1735) 2mm_4_23	25mer
491	GAGATAAAGCGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_4_6	25mer
492	GAGATGAAACGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_4_9	25mer
493	GAGGTAAAGCAGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_6_11	25mer
494	GAGGTAAAGCGAAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_6_12	25mer
495	GAGGTAAAGCGGAACTAACCCCTGTA	SHANK3 H22A(+1711+1735) 2mm_6_17	25mer
496	GAGGTAAAGCGGAACTGACCCTATA	SHANK3 H22A(+1711+1735) 2mm_6_23	25mer
497	GAGGTAAAACGGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_6_9	25mer
498	GAGGTGAAACAGAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_9_11	25mer
499	GAGGTGAAACGAAACTGACCCTGTA	SHANK3 H22A(+1711+1735) 2mm_9_12	25mer
500	GAGGTGAAACGGAACTAACCCCTGTA	SHANK3 H22A(+1711+1735) 2mm_9_17	25mer
501	GAGGTGAAACGGAACTGACCCTATA	SHANK3 H22A(+1711+1735) 2mm_9_23	25mer
502	GAGGTGAAGCGGAACTGACCCTATA	SHANK3 H22A(+1711+1735) mm1	25mer
503	TGAGGTGAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 1mm_1	25mer
504	GGAGGTGAATCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 1mm_10	25mer
505	GGAGGTGAAGTGGAAGTACCCTGT	SHANK3 H22A(+1712+1736) 1mm_11	25mer
506	GGAGGTGAAGCTGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 1mm_12	25mer
507	GGAGGTGAAGCGTAACTGACCCTGT	SHANK3 H22A(+1712+1736) 1mm_13	25mer
508	GGAGGTGAAGCGGAATTGACCCTGT	SHANK3 H22A(+1712+1736) 1mm_16	25mer
509	GGAGGTGAAGCGGAACTTACCCTGT	SHANK3 H22A(+1712+1736) 1mm_18	25mer
510	GTAGGTGAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 1mm_2	25mer
511	GGAGGTGAAGCGGAACTGATCCTGT	SHANK3 H22A(+1712+1736) 1mm_20	25mer
512	GGAGGTGAAGCGGAACTGACTCTGT	SHANK3 H22A(+1712+1736) 1mm_21	25mer
513	GGAGGTGAAGCGGAACTGACCTTGT	SHANK3 H22A(+1712+1736) 1mm_22	25mer

514	GGAGGTGAAGCGGAACTGACCCTTT	SHANK3 H22A(+1712+1736) 1mm_24	25mer
515	GGATGTGAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 1mm_4	25mer
516	GGAGTTGAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 1mm_5	25mer
517	GGAGGTTAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 1mm_7	25mer
518	AGAGGTGAAACGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_1_10	25mer
519	AGAGGTGAAGCAGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_1_12	25mer
520	AGAGGTGAAGCGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_1_13	25mer
521	AGAGGTGAAGCGGAACTAACCCTGT	SHANK3 H22A(+1712+1736) 2mm_1_18	25mer
522	AAAGGTGAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_1_2	25mer
523	AGAGGTGAAGCGGAACTGACCCTAT	SHANK3 H22A(+1712+1736) 2mm_1_24	25mer
524	AGAAGTGAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_1_4	25mer
525	AGAGATGAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_1_5	25mer
526	AGAGGTAAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_1_7	25mer
527	GGAGGTGAAACAGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_10_12	25mer
528	GGAGGTGAAACGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_10_13	25mer
529	GGAGGTGAAACGGAACTAACCCTGT	SHANK3 H22A(+1712+1736) 2mm_10_18	25mer
530	GGAGGTGAAACGGAACTGACCCTAT	SHANK3 H22A(+1712+1736) 2mm_10_24	25mer
531	GGAGGTGAAGCAAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_12_13	25mer
532	GGAGGTGAAGCAGAACTAACCCTGT	SHANK3 H22A(+1712+1736) 2mm_12_18	25mer
533	GGAGGTGAAGCAGAACTGACCCTAT	SHANK3 H22A(+1712+1736) 2mm_12_24	25mer
534	GGAGGTGAAGCGAACTAACCCTGT	SHANK3 H22A(+1712+1736) 2mm_13_18	25mer
535	GGAGGTGAAGCGAACTGACCCTAT	SHANK3 H22A(+1712+1736) 2mm_13_24	25mer
536	GAAGGTGAAACGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_2_10	25mer
537	GAAGGTGAAGCAGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_2_12	25mer
538	GAAGGTGAAGCGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_2_13	25mer
539	GAAGGTGAAGCGGAACTAACCCTGT	SHANK3 H22A(+1712+1736) 2mm_2_18	25mer
540	GAAGGTGAAGCGGAACTGACCCTAT	SHANK3 H22A(+1712+1736) 2mm_2_24	25mer
541	GAAAGTGAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_2_4	25mer

542	GAAGATGAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_2_5	25mer
543	GAAGGTAAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_2_7	25mer
544	GGAAGTGAACCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_4_10	25mer
545	GGAAGTGAAGCAGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_4_12	25mer
546	GGAAGTGAAGCGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_4_13	25mer
547	GGAAGTGAAGCGGAACTAACCCTGT	SHANK3 H22A(+1712+1736) 2mm_4_18	25mer
548	GGAAGTGAAGCGGAACTGACCCTAT	SHANK3 H22A(+1712+1736) 2mm_4_24	25mer
549	GGAATGAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_4_5	25mer
550	GGAAGTAAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_4_7	25mer
551	GGAGATGAAACCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_5_10	25mer
552	GGAGATGAAGCAGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_5_12	25mer
553	GGAGATGAAGCGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_5_13	25mer
554	GGAGATGAAGCGGAACTAACCCTGT	SHANK3 H22A(+1712+1736) 2mm_5_18	25mer
555	GGAGATGAAGCGGAACTGACCCTAT	SHANK3 H22A(+1712+1736) 2mm_5_24	25mer
556	GGAGATAAAGCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_5_7	25mer
557	GGAGGTAAAACCGGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_7_10	25mer
558	GGAGGTAAAGCAGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_7_12	25mer
559	GGAGGTAAAGCGAACTGACCCTGT	SHANK3 H22A(+1712+1736) 2mm_7_13	25mer
560	GGAGGTAAAGCGGAACTAACCCTGT	SHANK3 H22A(+1712+1736) 2mm_7_18	25mer
561	GGAGGTAAAGCGGAACTGACCCTAT	SHANK3 H22A(+1712+1736) 2mm_7_24	25mer
562	GGAGGTGAAGCGGAACTGACCCTAT	SHANK3 H22A(+1712+1736) mm1	25mer
563	AGGAGGTGAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737)	25mer
564	AGGAGGTGAATCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 1mm_11	25mer
565	AGGAGGTGAAGTGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 1mm_12	25mer
566	AGGAGGTGAAGCTGAACTGACCCTG	SHANK3 H22A(+1713+1737) 1mm_13	25mer
567	AGGAGGTGAAGCGTAACTGACCCTG	SHANK3 H22A(+1713+1737) 1mm_14	25mer
568	AGGAGGTGAAGCGGAATTGACCCTG	SHANK3 H22A(+1713+1737) 1mm_17	25mer
569	AGGAGGTGAAGCGGAACTTACCCTG	SHANK3 H22A(+1713+1737) 1mm_19	25mer
570	ATGAGGTGAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 1mm_2	25mer
571	AGGAGGTGAAGCGGAACTGATCCTG	SHANK3 H22A(+1713+1737) 1mm_21	25mer
572	AGGAGGTGAAGCGGAACTGACTCTG	SHANK3 H22A(+1713+1737) 1mm_22	25mer

573	AGGAGGTGAAGCGGAACTGACCTTG	SHANK3 H22A(+1713+1737) 1mm_23	25mer
574	AGTAGGTGAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 1mm_3	25mer
575	AGGATGTGAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 1mm_5	25mer
576	AGGAGTTGAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 1mm_6	25mer
577	AGGAGGTTAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 1mm_8	25mer
578	AGGAGGTGAAACAGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_11_13	25mer
579	AGGAGGTGAAACGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_11_14	25mer
580	AGGAGGTGAAACGGAACTAACCCCTG	SHANK3 H22A(+1713+1737) 2mm_11_19	25mer
581	AGGAGGTGAAACGGAACTGACCCTA	SHANK3 H22A(+1713+1737) 2mm_11_25	25mer
582	AGGAGGTGAAGCAAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_13_14	25mer
583	AGGAGGTGAAGCAGAACTAACCCCTG	SHANK3 H22A(+1713+1737) 2mm_13_19	25mer
584	AGGAGGTGAAGCAGAACTGACCCTA	SHANK3 H22A(+1713+1737) 2mm_13_25	25mer
585	AGGAGGTGAAGCGAACTAACCCCTG	SHANK3 H22A(+1713+1737) 2mm_14_19	25mer
586	AGGAGGTGAAGCGAACTGACCCTA	SHANK3 H22A(+1713+1737) 2mm_14_25	25mer
587	AAGAGGTGAAACGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_2_11	25mer
588	AAGAGGTGAAGCAGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_2_13	25mer
589	AAGAGGTGAAGCGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_2_14	25mer
590	AAGAGGTGAAGCGGAACTAACCCCTG	SHANK3 H22A(+1713+1737) 2mm_2_19	25mer
591	AAGAGGTGAAGCGGAACTGACCCTA	SHANK3 H22A(+1713+1737) 2mm_2_25	25mer
592	AAAAGGTGAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_2_3	25mer
593	AAGAAGTGAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_2_5	25mer
594	AAGAGATGAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_2_6	25mer
595	AAGAGGTAAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_2_8	25mer
596	AGAAGGTGAAACGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_3_11	25mer
597	AGAAGGTGAAGCAGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_3_13	25mer
598	AGAAGGTGAAGCGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_3_14	25mer
599	AGAAGGTGAAGCGGAACTAACCCCTG	SHANK3 H22A(+1713+1737) 2mm_3_19	25mer
600	AGAAGGTGAAGCGGAACTGACCCTA	SHANK3 H22A(+1713+1737) 2mm_3_25	25mer

601	AGAAAGTGAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_3_5	25mer
602	AGAAGATGAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_3_6	25mer
603	AGAAGGTAAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_3_8	25mer
604	AGGAAGTGAACCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_5_11	25mer
605	AGGAAGTGAAGCAGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_5_13	25mer
606	AGGAAGTGAAGCGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_5_14	25mer
607	AGGAAGTGAAGCGGAACTAACCCCTG	SHANK3 H22A(+1713+1737) 2mm_5_19	25mer
608	AGGAAGTGAAGCGGAACTGACCCTA	SHANK3 H22A(+1713+1737) 2mm_5_25	25mer
609	AGGAAATGAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_5_6	25mer
610	AGGAAGTAAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_5_8	25mer
611	AGGAGATGAAACCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_6_11	25mer
612	AGGAGATGAAGCAGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_6_13	25mer
613	AGGAGATGAAGCGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_6_14	25mer
614	AGGAGATGAAGCGGAACTAACCCCTG	SHANK3 H22A(+1713+1737) 2mm_6_19	25mer
615	AGGAGATGAAGCGGAACTGACCCTA	SHANK3 H22A(+1713+1737) 2mm_6_25	25mer
616	AGGAGATAAAGCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_6_8	25mer
617	AGGAGGTAAAACCGGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_8_11	25mer
618	AGGAGGTAAAGCAGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_8_13	25mer
619	AGGAGGTAAAGCGAACTGACCCTG	SHANK3 H22A(+1713+1737) 2mm_8_14	25mer
620	AGGAGGTAAAGCGGAACTAACCCCTG	SHANK3 H22A(+1713+1737) 2mm_8_19	25mer
621	AGGAGGTAAAGCGGAACTGACCCTA	SHANK3 H22A(+1713+1737) 2mm_8_25	25mer
622	AGGAGGTGAAGCGGAACTGACCCTA	SHANK3 H22A(+1713+1737) mm1	25mer
623	AAGGAGGTGAATCGGAACTGACCCT	SHANK3 H22A(+1714+1738) 1mm_12	25mer
624	AAGGAGGTGAAGTGGAAGTGAACCT	SHANK3 H22A(+1714+1738) 1mm_13	25mer
625	AAGGAGGTGAAGCTGAAGTGAACCT	SHANK3 H22A(+1714+1738) 1mm_14	25mer
626	AAGGAGGTGAAGCGTAAGTGAACCT	SHANK3 H22A(+1714+1738) 1mm_15	25mer
627	AAGGAGGTGAAGCGGAATTGAACCT	SHANK3 H22A(+1714+1738) 1mm_18	25mer
628	AAGGAGGTGAAGCGGAATTACCT	SHANK3 H22A(+1714+1738) 1mm_20	25mer
629	AAGGAGGTGAAGCGGAAGTGAACCT	SHANK3 H22A(+1714+1738) 1mm_22	25mer
630	AAGGAGGTGAAGCGGAAGTGAACCT	SHANK3 H22A(+1714+1738) 1mm_23	25mer
631	AAGGAGGTGAAGCGGAAGTGAACCT	SHANK3 H22A(+1714+1738) 1mm_24	25mer

632	AATGAGGTGAAGCGGAACTGACCCT	SHANK3 H22A(+1714+1738) 1mm_3	25mer
633	AAGTAGGTGAAGCGGAACTGACCCT	SHANK3 H22A(+1714+1738) 1mm_4	25mer
634	AAGGATGTGAAGCGGAACTGACCCT	SHANK3 H22A(+1714+1738) 1mm_6	25mer
635	AAGGAGTTGAAGCGGAACTGACCCT	SHANK3 H22A(+1714+1738) 1mm_7	25mer
636	AAGGAGGTTAAGCGGAACTGACCCT	SHANK3 H22A(+1714+1738) 1mm_9	25mer
637	AAGGAGGTGAAGCGGAACTAACCCCT	SHANK3 H22A(+1714+1738) mm1	25mer
638	AAGGAGGTGAAGCGGAACTAACCCCT	SHANK3 H22A(+1714+1738) mm2	25mer
639	AAAGGAGGTGAAGCGGAACTGACCC	SHANK3 H22A(+1715+1739)	25mer
640	AAAGGAGGTGAAGCGGAACTGACCC	SHANK3 H22A(+1715+1739) 1mm_10	25mer
641	AAAGGAGGTGAATCGGAACTGACCC	SHANK3 H22A(+1715+1739) 1mm_13	25mer
642	AAAGGAGGTGAAGTGGAACTGACCC	SHANK3 H22A(+1715+1739) 1mm_14	25mer
643	AAAGGAGGTGAAGCTGAACTGACCC	SHANK3 H22A(+1715+1739) 1mm_15	25mer
644	AAAGGAGGTGAAGCGTAACTGACCC	SHANK3 H22A(+1715+1739) 1mm_16	25mer
645	AAAGGAGGTGAAGCGGAATTGACCC	SHANK3 H22A(+1715+1739) 1mm_19	25mer
646	AAAGGAGGTGAAGCGGAACTTACCC	SHANK3 H22A(+1715+1739) 1mm_21	25mer
647	AAAGGAGGTGAAGCGGAACTGATCC	SHANK3 H22A(+1715+1739) 1mm_23	25mer
648	AAAGGAGGTGAAGCGGAACTGACTC	SHANK3 H22A(+1715+1739) 1mm_24	25mer
649	AAAGGAGGTGAAGCGGAACTGACCT	SHANK3 H22A(+1715+1739) 1mm_25	25mer
650	AAATGAGGTGAAGCGGAACTGACCC	SHANK3 H22A(+1715+1739) 1mm_4	25mer
651	AAAGTAGGTGAAGCGGAACTGACCC	SHANK3 H22A(+1715+1739) 1mm_5	25mer
652	AAAGGATGTGAAGCGGAACTGACCC	SHANK3 H22A(+1715+1739) 1mm_7	25mer
653	AAAGGAGTTGAAGCGGAACTGACCC	SHANK3 H22A(+1715+1739) 1mm_8	25mer
654	AAAGGAGGTGAAGCGGAACTAACCC	SHANK3 H22A(+1715+1739) mm1	25mer
655	AAAGGAGGTGAAGCGGAACTAACCC	SHANK3 H22A(+1715+1739) mm2	25mer
656	AAAAGGAGGTGAAGCGGAACTGACC	SHANK3 H22A(+1716+1740)	25mer
657	AAAAGGAGGTGAAGCGGAACTGACC	SHANK3 H22A(+1716+1740) 1mm_11	25mer
658	AAAAGGAGGTGAATCGGAACTGACC	SHANK3 H22A(+1716+1740) 1mm_14	25mer
659	AAAAGGAGGTGAAGTGGAACTGACC	SHANK3 H22A(+1716+1740) 1mm_15	25mer
660	AAAAGGAGGTGAAGCTGAACTGACC	SHANK3 H22A(+1716+1740) 1mm_16	25mer
661	AAAAGGAGGTGAAGCGTAACTGACC	SHANK3 H22A(+1716+1740) 1mm_17	25mer
662	AAAAGGAGGTGAAGCGGAATTGACC	SHANK3 H22A(+1716+1740) 1mm_20	25mer
663	AAAAGGAGGTGAAGCGGAACTTACC	SHANK3 H22A(+1716+1740) 1mm_22	25mer
664	AAAAGGAGGTGAAGCGGAACTGATC	SHANK3 H22A(+1716+1740) 1mm_24	25mer
665	AAAAGGAGGTGAAGCGGAACTGACT	SHANK3 H22A(+1716+1740) 1mm_25	25mer
666	AAAATGAGGTGAAGCGGAACTGACC	SHANK3 H22A(+1716+1740) 1mm_5	25mer
667	AAAAGTAGGTGAAGCGGAACTGACC	SHANK3 H22A(+1716+1740) 1mm_6	25mer
668	AAAAGGATGTGAAGCGGAACTGACC	SHANK3 H22A(+1716+1740) 1mm_8	25mer
669	AAAAGGAGTTGAAGCGGAACTGACC	SHANK3 H22A(+1716+1740) 1mm_9	25mer
670	AAAAGGAGGTGAAGCGGAACTAACCC	SHANK3 H22A(+1716+1740) mm1	25mer
671	AAAAGGAGGTGAAGCGGAACTAACCC	SHANK3 H22A(+1716+1740) mm2	25mer
672	TAAAAGGAGGTGAAGCGGAACTGAC	SHANK3 H22A(+1717+1741) 1mm_1	25mer

673	CAAAAGGAGTTGAAGCGGAAGTAC	SHANK3 H22A(+1717+1741) 1mm_10	25mer
674	CAAAAGGAGGTGAAGCGGAAGTAC	SHANK3 H22A(+1717+1741) 1mm_12	25mer
675	CAAAAGGAGGTGAATCGGAAGTAC	SHANK3 H22A(+1717+1741) 1mm_15	25mer
676	CAAAAGGAGGTGAAGTGGAACTGAC	SHANK3 H22A(+1717+1741) 1mm_16	25mer
677	CAAAAGGAGGTGAAGCTGAACTGAC	SHANK3 H22A(+1717+1741) 1mm_17	25mer
678	CAAAAGGAGGTGAAGCGTAACTGAC	SHANK3 H22A(+1717+1741) 1mm_18	25mer
679	CAAAAGGAGGTGAAGCGGAATTGAC	SHANK3 H22A(+1717+1741) 1mm_21	25mer
680	CAAAAGGAGGTGAAGCGGAAGTTAC	SHANK3 H22A(+1717+1741) 1mm_23	25mer
681	CAAAAGGAGGTGAAGCGGAAGTAT	SHANK3 H22A(+1717+1741) 1mm_25	25mer
682	CAAAATGAGGTGAAGCGGAAGTAC	SHANK3 H22A(+1717+1741) 1mm_6	25mer
683	CAAAAGTAGGTGAAGCGGAAGTAC	SHANK3 H22A(+1717+1741) 1mm_7	25mer
684	CAAAAGGATGTGAAGCGGAAGTAC	SHANK3 H22A(+1717+1741) 1mm_9	25mer
685	CAAAAGGAGGTGAAGCGGAAGTAA	SHANK3 H22A(+1717+1741) mm1	25mer
686	CAAAAGGAGGTGAAGCGGAAGTAA	SHANK3 H22A(+1717+1741) mm2	25mer
687	ACAAAAGGAGGTGAAGCGGAAGTGA	SHANK3 H22A(+1718+1742)	25mer
688	ACAAAAGGATGTGAAGCGGAAGTGA	SHANK3 H22A(+1718+1742) 1mm_10	25mer
689	ACAAAAGGAGTTGAAGCGGAAGTGA	SHANK3 H22A(+1718+1742) 1mm_11	25mer
690	ACAAAAGGAGGTGAAGCGGAAGTGA	SHANK3 H22A(+1718+1742) 1mm_13	25mer
691	ACAAAAGGAGGTGAATCGGAAGTGA	SHANK3 H22A(+1718+1742) 1mm_16	25mer
692	ACAAAAGGAGGTGAAGTGGAACTGA	SHANK3 H22A(+1718+1742) 1mm_17	25mer
693	ACAAAAGGAGGTGAAGCTGAACTGA	SHANK3 H22A(+1718+1742) 1mm_18	25mer
694	ACAAAAGGAGGTGAAGCGTAACTGA	SHANK3 H22A(+1718+1742) 1mm_19	25mer
695	ATAAAAGGAGGTGAAGCGGAAGTGA	SHANK3 H22A(+1718+1742) 1mm_2	25mer
696	ACAAAAGGAGGTGAAGCGGAATTGA	SHANK3 H22A(+1718+1742) 1mm_22	25mer
697	ACAAAAGGAGGTGAAGCGGAAGTTA	SHANK3 H22A(+1718+1742) 1mm_24	25mer
698	ACAAAATGAGGTGAAGCGGAAGTGA	SHANK3 H22A(+1718+1742) 1mm_7	25mer
699	ACAAAAGTAGGTGAAGCGGAAGTGA	SHANK3 H22A(+1718+1742) 1mm_8	25mer
700	ACAAAAGGAGGTGAAGCGGAAGTAA	SHANK3 H22A(+1718+1742) mm1	25mer
701	ACAAAAGGAGGTGAAGCGGAAGTAA	SHANK3 H22A(+1718+1742) mm2	25mer
702	TACAAAAGGAGGTGAAGCGGAAGTGA	SHANK3 H22A(+1719+1743)	25mer
703	TACAAAAGGATGTGAAGCGGAAGTGA	SHANK3 H22A(+1719+1743) 1mm_11	25mer
704	TACAAAAGGAGTTGAAGCGGAAGTGA	SHANK3 H22A(+1719+1743) 1mm_12	25mer
705	TACAAAAGGAGGTGAAGCGGAAGTGA	SHANK3 H22A(+1719+1743) 1mm_14	25mer
706	TACAAAAGGAGGTGAATCGGAAGTGA	SHANK3 H22A(+1719+1743) 1mm_17	25mer
707	TACAAAAGGAGGTGAAGTGGAACTGA	SHANK3 H22A(+1719+1743) 1mm_18	25mer
708	TACAAAAGGAGGTGAAGCTGAACTGA	SHANK3 H22A(+1719+1743) 1mm_19	25mer
709	TACAAAAGGAGGTGAAGCGTAACTGA	SHANK3 H22A(+1719+1743) 1mm_20	25mer
710	TACAAAAGGAGGTGAAGCGGAATTG	SHANK3 H22A(+1719+1743) 1mm_23	25mer
711	TATAAAAGGAGGTGAAGCGGAAGTGA	SHANK3 H22A(+1719+1743) 1mm_3	25mer
712	TACAAAATGAGGTGAAGCGGAAGTGA	SHANK3 H22A(+1719+1743) 1mm_8	25mer
713	TACAAAAGTAGGTGAAGCGGAAGTGA	SHANK3 H22A(+1719+1743) 1mm_9	25mer

714	TACAAAAGGAGGTGAAGCGGAACTA	SHANK3 H22A(+1719+1743) mm1	25mer
715	TACAAAAGGAGGTGAAGCGAACTA	SHANK3 H22A(+1719+1743) mm2	25mer
716	ATACAAAAGTAGGTGAAGCGGAACT	SHANK3 H22A(+1720+1744) 1mm_10	25mer
717	ATACAAAAGGATGTGAAGCGGAACT	SHANK3 H22A(+1720+1744) 1mm_12	25mer
718	ATACAAAAGGAGTTGAAGCGGAACT	SHANK3 H22A(+1720+1744) 1mm_13	25mer
719	ATACAAAAGGAGGTTAAGCGGAACT	SHANK3 H22A(+1720+1744) 1mm_15	25mer
720	ATACAAAAGGAGGTGAATCGGAACT	SHANK3 H22A(+1720+1744) 1mm_18	25mer
721	ATACAAAAGGAGGTGAAGTGGAAC	SHANK3 H22A(+1720+1744) 1mm_19	25mer
722	ATACAAAAGGAGGTGAAGCTGAAC	SHANK3 H22A(+1720+1744) 1mm_20	25mer
723	ATACAAAAGGAGGTGAAGCGTAACT	SHANK3 H22A(+1720+1744) 1mm_21	25mer
724	ATACAAAAGGAGGTGAAGCGGAATT	SHANK3 H22A(+1720+1744) 1mm_24	25mer
725	ATATAAAGGAGGTGAAGCGGAACT	SHANK3 H22A(+1720+1744) 1mm_4	25mer
726	ATACAAAATGAGGTGAAGCGGAACT	SHANK3 H22A(+1720+1744) 1mm_9	25mer
727	ATACAAAAGGAGGTGAAACGAACT	SHANK3 H22A(+1720+1744) 2mm_18_21	25mer
728	ATACAAAAGGAGGTGAAGCGGAACT	SHANK3 H22A(+1720+1744) mm1	25mer
729	ATACAAAAGGAGGTGAAGCGAACT	SHANK3 H22A(+1720+1744) mm2	25mer
730	TAAAAACCCAAATTTAAC	SHANK3 H22A(+1689+1706) 1mm_15	18mer
731	TAAAAACCCAAATTGAAT	SHANK3 H22A(+1689+1706) 1mm_18	18mer
732	TAAAAATCCAAATTGAAC	SHANK3 H22A(+1689+1706) 1mm_7	18mer
733	TAAAAACTCAAATTGAAC	SHANK3 H22A(+1689+1706) 1mm_8	18mer
734	TAAAAACCTAAATTGAAC	SHANK3 H22A(+1689+1706) 1mm_9	18mer
735	TTAAAAACCTAAATTGAA	SHANK3 H22A(+1690+1707) 1mm_10	18mer
736	TTAAAAACCCAAATTTAA	SHANK3 H22A(+1690+1707) 1mm_16	18mer
737	TTAAAAATCCAAATTGAA	SHANK3 H22A(+1690+1707) 1mm_8	18mer
738	TTAAAAACTCAAATTGAA	SHANK3 H22A(+1690+1707) 1mm_9	18mer
739	TTTAAAAACCCAAATTGA	SHANK3 H22A(+1691+1708) 1mm_1	18mer
740	GTTAAAAACTCAAATTGA	SHANK3 H22A(+1691+1708) 1mm_10	18mer
741	GTTAAAAACCTAAATTGA	SHANK3 H22A(+1691+1708) 1mm_11	18mer
742	GTTAAAAACCCAAATTTA	SHANK3 H22A(+1691+1708) 1mm_17	18mer
743	GTTAAAAATCCAAATTGA	SHANK3 H22A(+1691+1708) 1mm_9	18mer
744	AGTTAAAAATCCAAATTG	SHANK3 H22A(+1692+1709) 1mm_10	18mer
745	AGTTAAAAACTCAAATTG	SHANK3 H22A(+1692+1709) 1mm_11	18mer
746	AGTTAAAAACCTAAATTG	SHANK3 H22A(+1692+1709) 1mm_12	18mer
747	AGTTAAAAACCCAAATTT	SHANK3 H22A(+1692+1709) 1mm_18	18mer
748	ATTTAAAAACCCAAATTG	SHANK3 H22A(+1692+1709) 1mm_2	18mer
749	AAGTTAAAAATCCAAATT	SHANK3 H22A(+1693+1710) 1mm_11	18mer
750	AAGTTAAAAACTCAAATT	SHANK3 H22A(+1693+1710) 1mm_12	18mer
751	AAGTTAAAAACCTAAATT	SHANK3 H22A(+1693+1710) 1mm_13	18mer
752	AATTTAAAAACCCAAATT	SHANK3 H22A(+1693+1710) 1mm_3	18mer
753	AAAGTTAAAAATCCAAAT	SHANK3 H22A(+1694+1711) 1mm_12	18mer

754	AAAGTTAAAAACTCAAAT	SHANK3 H22A(+1694+1711) 1mm_13	18mer
755	AAAGTTAAAAACCTAAAT	SHANK3 H22A(+1694+1711) 1mm_14	18mer
756	AAATTTAAAAACCCAAAT	SHANK3 H22A(+1694+1711) 1mm_4	18mer
757	TAAAGTTAAAAATCCAAA	SHANK3 H22A(+1695+1712) 1mm_13	18mer
758	TAAAGTTAAAAACTCAAA	SHANK3 H22A(+1695+1712) 1mm_14	18mer
759	TAAAGTTAAAAACCTAAA	SHANK3 H22A(+1695+1712) 1mm_15	18mer
760	TAAATTTAAAAACCCAAA	SHANK3 H22A(+1695+1712) 1mm_5	18mer
761	TTAAAGTTAAAAACCCAA	SHANK3 H22A(+1696+1713) 1mm_1	18mer
762	GTAAAGTTAAAAATCCAA	SHANK3 H22A(+1696+1713) 1mm_14	18mer
763	GTAAAGTTAAAAACTCAA	SHANK3 H22A(+1696+1713) 1mm_15	18mer
764	GTAAAGTTAAAAACCTAA	SHANK3 H22A(+1696+1713) 1mm_16	18mer
765	GTAAATTTAAAAACCCAA	SHANK3 H22A(+1696+1713) 1mm_6	18mer
766	TGTAAAGTTAAAAATCCA	SHANK3 H22A(+1697+1714) 1mm_15	18mer
767	TGTAAAGTTAAAAACTCA	SHANK3 H22A(+1697+1714) 1mm_16	18mer
768	TGTAAAGTTAAAAACCTA	SHANK3 H22A(+1697+1714) 1mm_17	18mer
769	TTTAAAGTTAAAAACCCA	SHANK3 H22A(+1697+1714) 1mm_2	18mer
770	TGTAAATTTAAAAACCCA	SHANK3 H22A(+1697+1714) 1mm_7	18mer
771	TTGTAAAGTTAAAAACCC	SHANK3 H22A(+1698+1715) 1mm_1	18mer
772	CTGTAAAGTTAAAAATCC	SHANK3 H22A(+1698+1715) 1mm_16	18mer
773	CTGTAAAGTTAAAAACTC	SHANK3 H22A(+1698+1715) 1mm_17	18mer
774	CTGTAAAGTTAAAAACCT	SHANK3 H22A(+1698+1715) 1mm_18	18mer
775	CTTTAAAGTTAAAAACCC	SHANK3 H22A(+1698+1715) 1mm_3	18mer
776	CTGTAAATTTAAAAACCC	SHANK3 H22A(+1698+1715) 1mm_8	18mer
777	TCTGTAAAGTTAAAAACC	SHANK3 H22A(+1699+1716) 1mm_1	18mer
778	CCTGTAAAGTTAAAAATC	SHANK3 H22A(+1699+1716) 1mm_17	18mer
779	CCTGTAAAGTTAAAAACT	SHANK3 H22A(+1699+1716) 1mm_18	18mer
780	CTTGTAAAGTTAAAAACC	SHANK3 H22A(+1699+1716) 1mm_2	18mer
781	CCTTTAAAGTTAAAAACC	SHANK3 H22A(+1699+1716) 1mm_4	18mer
782	CCTGTAAATTTAAAAACC	SHANK3 H22A(+1699+1716) 1mm_9	18mer
783	TCCTGTAAAGTTAAAAAC	SHANK3 H22A(+1700+1717) 1mm_1	18mer
784	CCCTGTAAATTTAAAAAC	SHANK3 H22A(+1700+1717) 1mm_10	18mer
785	CCCTGTAAAGTTAAAAAT	SHANK3 H22A(+1700+1717) 1mm_18	18mer
786	CTCTGTAAAGTTAAAAAC	SHANK3 H22A(+1700+1717) 1mm_2	18mer
787	CCTTGTAAAGTTAAAAAC	SHANK3 H22A(+1700+1717) 1mm_3	18mer
788	CCCTTTAAAGTTAAAAAC	SHANK3 H22A(+1700+1717) 1mm_5	18mer
789	ACCCTGTAAATTTAAAAA	SHANK3 H22A(+1701+1718) 1mm_11	18mer
790	ATCCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1718) 1mm_2	18mer
791	ACTCTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1718) 1mm_3	18mer
792	ACCTTGTAAAGTTAAAAA	SHANK3 H22A(+1701+1718) 1mm_4	18mer
793	ACCCTTTAAAGTTAAAAA	SHANK3 H22A(+1701+1718) 1mm_6	18mer
794	TACCCTGTAAAGTTAAAA	SHANK3 H22A(+1702+1719) 1mm_1	18mer

795	GACCCTGTAAATTTAAAA	SHANK3 H22A(+1702+1719) 1mm_12	18mer
796	GATCCTGTAAAGTTAAAA	SHANK3 H22A(+1702+1719) 1mm_3	18mer
797	GACTCTGTAAAGTTAAAA	SHANK3 H22A(+1702+1719) 1mm_4	18mer
798	GACCTTGTAAAGTTAAAA	SHANK3 H22A(+1702+1719) 1mm_5	18mer
799	GACCCTTTAAAGTTAAAA	SHANK3 H22A(+1702+1719) 1mm_7	18mer
800	TGACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1720)	18mer
801	TGACCCTGTAAATTTAAA	SHANK3 H22A(+1703+1720) 1mm_13	18mer
802	TTACCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1720) 1mm_2	18mer
803	TGATCCTGTAAAGTTAAA	SHANK3 H22A(+1703+1720) 1mm_4	18mer
804	TGACTCTGTAAAGTTAAA	SHANK3 H22A(+1703+1720) 1mm_5	18mer
805	TGACCTTGTAAAGTTAAA	SHANK3 H22A(+1703+1720) 1mm_6	18mer
806	TGACCCTTTAAAGTTAAA	SHANK3 H22A(+1703+1720) 1mm_8	18mer
807	TGACCCTGTAAATTTAAA	SHANK3 H22A(+1703+1720) mm1	18mer
808	CTGACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1721)	18mer
809	TTGACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1721) 1mm_1	18mer
810	CTGACCCTGTAAATTTAA	SHANK3 H22A(+1704+1721) 1mm_14	18mer
811	CTTACCCTGTAAAGTTAA	SHANK3 H22A(+1704+1721) 1mm_3	18mer
812	CTGATCCTGTAAAGTTAA	SHANK3 H22A(+1704+1721) 1mm_5	18mer
813	CTGACTCTGTAAAGTTAA	SHANK3 H22A(+1704+1721) 1mm_6	18mer
814	CTGACCTTGTAAAGTTAA	SHANK3 H22A(+1704+1721) 1mm_7	18mer
815	CTGACCCTTTAAAGTTAA	SHANK3 H22A(+1704+1721) 1mm_9	18mer
816	CTGACCCTGTAAAATTA	SHANK3 H22A(+1704+1721) mm1	18mer
817	ACTGACCCTGTAAAGTTA	SHANK3 H22A(+1705+1722)	18mer
818	ACTGACCCTTTAAAGTTA	SHANK3 H22A(+1705+1722) 1mm_10	18mer
819	ACTGACCCTGTAAATTTA	SHANK3 H22A(+1705+1722) 1mm_15	18mer
820	ATTGACCCTGTAAAGTTA	SHANK3 H22A(+1705+1722) 1mm_2	18mer
821	ACTTACCCTGTAAAGTTA	SHANK3 H22A(+1705+1722) 1mm_4	18mer
822	ACTGATCCTGTAAAGTTA	SHANK3 H22A(+1705+1722) 1mm_6	18mer
823	ACTGACTCTGTAAAGTTA	SHANK3 H22A(+1705+1722) 1mm_7	18mer
824	ACTGACCTTGTAAAGTTA	SHANK3 H22A(+1705+1722) 1mm_8	18mer
825	ACTGACCCTGTAAAATTA	SHANK3 H22A(+1705+1722) mm1	18mer
826	AACTGACCCTGTAAAGTT	SHANK3 H22A(+1706+1723)	18mer
827	AACTGACCCTTTAAAGTT	SHANK3 H22A(+1706+1723) 1mm_11	18mer
828	AACTGACCCTGTAAATTT	SHANK3 H22A(+1706+1723) 1mm_16	18mer
829	AATGACCCTGTAAAGTT	SHANK3 H22A(+1706+1723) 1mm_3	18mer
830	AACTTACCCTGTAAAGTT	SHANK3 H22A(+1706+1723) 1mm_5	18mer
831	AACTGATCCTGTAAAGTT	SHANK3 H22A(+1706+1723) 1mm_7	18mer
832	AACTGACTCTGTAAAGTT	SHANK3 H22A(+1706+1723) 1mm_8	18mer
833	AACTGACCTTGTAAAGTT	SHANK3 H22A(+1706+1723) 1mm_9	18mer
834	AACTGACCCTGTAAAATT	SHANK3 H22A(+1706+1723) mm1	18mer
835	GAACTGACCCTGTAAAGT	SHANK3 H22A(+1707+1724)	18mer

836	TAAGTACCCCTGTAAAGT	SHANK3 H22A(+1707+1724) 1mm_1	18mer
837	GAACTGACCTTGTAAAGT	SHANK3 H22A(+1707+1724) 1mm_10	18mer
838	GAACTGACCCCTTTAAAGT	SHANK3 H22A(+1707+1724) 1mm_12	18mer
839	GAACTGACCCCTGTAAATT	SHANK3 H22A(+1707+1724) 1mm_17	18mer
840	GAATTGACCCCTGTAAAGT	SHANK3 H22A(+1707+1724) 1mm_4	18mer
841	GAACTTACCCTGTAAAGT	SHANK3 H22A(+1707+1724) 1mm_6	18mer
842	GAACTGATCCTGTAAAGT	SHANK3 H22A(+1707+1724) 1mm_8	18mer
843	GAACTGACTCTGTAAAGT	SHANK3 H22A(+1707+1724) 1mm_9	18mer
844	GAACTGACCCCTGTAAAAT	SHANK3 H22A(+1707+1724) mm1	18mer
845	GGAAGTACCCCTGTAAAG	SHANK3 H22A(+1708+1725)	18mer
846	TGAAGTACCCCTGTAAAG	SHANK3 H22A(+1708+1725) 1mm_1	18mer
847	GGAAGTACTCTGTAAAG	SHANK3 H22A(+1708+1725) 1mm_10	18mer
848	GGAAGTACCTTGTAAAG	SHANK3 H22A(+1708+1725) 1mm_11	18mer
849	GGAAGTACCCCTTTAAAG	SHANK3 H22A(+1708+1725) 1mm_13	18mer
850	GGAAGTACCCCTGTAAAT	SHANK3 H22A(+1708+1725) 1mm_18	18mer
851	GTAAGTACCCCTGTAAAG	SHANK3 H22A(+1708+1725) 1mm_2	18mer
852	GGAATTGACCCCTGTAAAG	SHANK3 H22A(+1708+1725) 1mm_5	18mer
853	GGAAGTACCCTGTAAAG	SHANK3 H22A(+1708+1725) 1mm_7	18mer
854	GGAAGTGATCCTGTAAAG	SHANK3 H22A(+1708+1725) 1mm_9	18mer
855	GGAAGTACCCCTGTAAAA	SHANK3 H22A(+1708+1725) mm1	18mer
856	CGGAAGTACCCCTGTAAA	SHANK3 H22A(+1709+1726)	18mer
857	TGGAAGTACCCCTGTAAA	SHANK3 H22A(+1709+1726) 1mm_1	18mer
858	CGGAAGTGATCCTGTAAA	SHANK3 H22A(+1709+1726) 1mm_10	18mer
859	CGGAAGTACTCTGTAAA	SHANK3 H22A(+1709+1726) 1mm_11	18mer
860	CGGAAGTACCTTGTAAA	SHANK3 H22A(+1709+1726) 1mm_12	18mer
861	CGGAAGTACCCCTTTAAA	SHANK3 H22A(+1709+1726) 1mm_14	18mer
862	CTGAAGTACCCCTGTAAA	SHANK3 H22A(+1709+1726) 1mm_2	18mer
863	CGTAAGTACCCCTGTAAA	SHANK3 H22A(+1709+1726) 1mm_3	18mer
864	CGGAATTGACCCCTGTAAA	SHANK3 H22A(+1709+1726) 1mm_6	18mer
865	CGGAAGTACCCTGTAAA	SHANK3 H22A(+1709+1726) 1mm_8	18mer
866	CGGAAGTACCCCTATAAA	SHANK3 H22A(+1709+1726) mm1	18mer
867	GCGGAAGTACCCCTGTAA	SHANK3 H22A(+1710+1727)	18mer
868	TCGGAAGTACCCCTGTAA	SHANK3 H22A(+1710+1727) 1mm_1	18mer
869	GCGGAAGTGATCCTGTAA	SHANK3 H22A(+1710+1727) 1mm_11	18mer
870	GCGGAAGTACTCTGTAA	SHANK3 H22A(+1710+1727) 1mm_12	18mer
871	GCGGAAGTACCTTGTAA	SHANK3 H22A(+1710+1727) 1mm_13	18mer
872	GCGGAAGTACCCCTTTAA	SHANK3 H22A(+1710+1727) 1mm_15	18mer
873	GTGGAAGTACCCCTGTAA	SHANK3 H22A(+1710+1727) 1mm_2	18mer
874	GCTGAAGTACCCCTGTAA	SHANK3 H22A(+1710+1727) 1mm_3	18mer
875	GCGTAAGTACCCCTGTAA	SHANK3 H22A(+1710+1727) 1mm_4	18mer
876	GCGGAATTGACCCCTGTAA	SHANK3 H22A(+1710+1727) 1mm_7	18mer

877	GCGGAACTTACCCTGTAA	SHANK3 H22A(+1710+1727) 1mm_9	18mer
878	GCGGAACTGACCCCTATAA	SHANK3 H22A(+1710+1727) mm1	18mer
879	AGCGGAACTGACCCCTGTA	SHANK3 H22A(+1711+1728)	18mer
880	AGCGGAACTTACCCTGTA	SHANK3 H22A(+1711+1728) 1mm_10	18mer
881	AGCGGAACTGATCCTGTA	SHANK3 H22A(+1711+1728) 1mm_12	18mer
882	AGCGGAACTGACTCTGTA	SHANK3 H22A(+1711+1728) 1mm_13	18mer
883	AGCGGAACTGACCTTGTA	SHANK3 H22A(+1711+1728) 1mm_14	18mer
884	AGCGGAACTGACCCCTTA	SHANK3 H22A(+1711+1728) 1mm_16	18mer
885	ATCGGAACTGACCCCTGTA	SHANK3 H22A(+1711+1728) 1mm_2	18mer
886	AGTGGAAGTACCCTGTA	SHANK3 H22A(+1711+1728) 1mm_3	18mer
887	AGCTGAACTGACCCCTGTA	SHANK3 H22A(+1711+1728) 1mm_4	18mer
888	AGCGTAACTGACCCCTGTA	SHANK3 H22A(+1711+1728) 1mm_5	18mer
889	AGCGGAATTGACCCCTGTA	SHANK3 H22A(+1711+1728) 1mm_8	18mer
890	AGCGGAACTGACCCCTATA	SHANK3 H22A(+1711+1728) mm1	18mer
891	AAGCGGAACTGACCCCTGT	SHANK3 H22A(+1712+1729)	18mer
892	AAGCGGAACTTACCCTGT	SHANK3 H22A(+1712+1729) 1mm_11	18mer
893	AAGCGGAACTGATCCTGT	SHANK3 H22A(+1712+1729) 1mm_13	18mer
894	AAGCGGAACTGACTCTGT	SHANK3 H22A(+1712+1729) 1mm_14	18mer
895	AAGCGGAACTGACCTTGT	SHANK3 H22A(+1712+1729) 1mm_15	18mer
896	AAGCGGAACTGACCCCTT	SHANK3 H22A(+1712+1729) 1mm_17	18mer
897	AATCGGAACTGACCCCTGT	SHANK3 H22A(+1712+1729) 1mm_3	18mer
898	AAGTGGAAGTACCCTGT	SHANK3 H22A(+1712+1729) 1mm_4	18mer
899	AAGCTGAACTGACCCCTGT	SHANK3 H22A(+1712+1729) 1mm_5	18mer
900	AAGCGTAACTGACCCCTGT	SHANK3 H22A(+1712+1729) 1mm_6	18mer
901	AAGCGGAATTGACCCCTGT	SHANK3 H22A(+1712+1729) 1mm_9	18mer
902	AAGCGGAACTGACCCCTAT	SHANK3 H22A(+1712+1729) mm1	18mer
903	GAAGCGGAACTGACCCCTG	SHANK3 H22A(+1713+1730)	18mer
904	TAAGCGGAACTGACCCCTG	SHANK3 H22A(+1713+1730) 1mm_1	18mer
905	GAAGCGGAATTGACCCCTG	SHANK3 H22A(+1713+1730) 1mm_10	18mer
906	GAAGCGGAACTTACCCTG	SHANK3 H22A(+1713+1730) 1mm_12	18mer
907	GAAGCGGAACTGATCCTG	SHANK3 H22A(+1713+1730) 1mm_14	18mer
908	GAAGCGGAACTGACTCTG	SHANK3 H22A(+1713+1730) 1mm_15	18mer
909	GAAGCGGAACTGACCTTG	SHANK3 H22A(+1713+1730) 1mm_16	18mer
910	GAAGCGGAACTGACCCCTT	SHANK3 H22A(+1713+1730) 1mm_18	18mer
911	GAATCGGAACTGACCCCTG	SHANK3 H22A(+1713+1730) 1mm_4	18mer
912	GAAGTGGAAGTACCCTG	SHANK3 H22A(+1713+1730) 1mm_5	18mer
913	GAAGCTGAACTGACCCCTG	SHANK3 H22A(+1713+1730) 1mm_6	18mer
914	GAAGCGTAACTGACCCCTG	SHANK3 H22A(+1713+1730) 1mm_7	18mer
915	GAAGCGGAACTGACCCTA	SHANK3 H22A(+1713+1730) mm1	18mer
916	TGAAGCGGAACTGACCCCT	SHANK3 H22A(+1714+1731)	18mer
917	TGAAGCGGAATTGACCCCT	SHANK3 H22A(+1714+1731) 1mm_11	18mer

918	TGAAGCGGAACTTACCCT	SHANK3 H22A(+1714+1731) 1mm_13	18mer
919	TGAAGCGGAACTGATCCT	SHANK3 H22A(+1714+1731) 1mm_15	18mer
920	TGAAGCGGAACTGACTCT	SHANK3 H22A(+1714+1731) 1mm_16	18mer
921	TGAAGCGGAACTGACCTT	SHANK3 H22A(+1714+1731) 1mm_17	18mer
922	TTAAGCGGAACTGACCCT	SHANK3 H22A(+1714+1731) 1mm_2	18mer
923	TGAATCGGAACTGACCCT	SHANK3 H22A(+1714+1731) 1mm_5	18mer
924	TGAAGTGGAAGTACCCT	SHANK3 H22A(+1714+1731) 1mm_6	18mer
925	TGAAGCTGAACTGACCCT	SHANK3 H22A(+1714+1731) 1mm_7	18mer
926	TGAAGCGTAACTGACCCT	SHANK3 H22A(+1714+1731) 1mm_8	18mer
927	TGAAGCGGAACTAACCCT	SHANK3 H22A(+1714+1731) mm1	18mer
928	GTGAAGCGGAACTGACCC	SHANK3 H22A(+1715+1732)	18mer
929	TTGAAGCGGAACTGACCC	SHANK3 H22A(+1715+1732) 1mm_1	18mer
930	GTGAAGCGGAATTGACCC	SHANK3 H22A(+1715+1732) 1mm_12	18mer
931	GTGAAGCGGAACTTACCC	SHANK3 H22A(+1715+1732) 1mm_14	18mer
932	GTGAAGCGGAACTGATCC	SHANK3 H22A(+1715+1732) 1mm_16	18mer
933	GTGAAGCGGAACTGACTC	SHANK3 H22A(+1715+1732) 1mm_17	18mer
934	GTGAAGCGGAACTGACCT	SHANK3 H22A(+1715+1732) 1mm_18	18mer
935	GTGAAGCGGAACTGACCC	SHANK3 H22A(+1715+1732) 1mm_3	18mer
936	GTGAATCGGAACTGACCC	SHANK3 H22A(+1715+1732) 1mm_6	18mer
937	GTGAAGTGGAAGTACCCT	SHANK3 H22A(+1715+1732) 1mm_7	18mer
938	GTGAAGCTGAACTGACCC	SHANK3 H22A(+1715+1732) 1mm_8	18mer
939	GTGAAGCGTAACTGACCC	SHANK3 H22A(+1715+1732) 1mm_9	18mer
940	GTGAAGCGGAACTAACCCT	SHANK3 H22A(+1715+1732) mm1	18mer
941	GGTGAAGCGGAACTGACC	SHANK3 H22A(+1716+1733)	18mer
942	TGTGAAGCGGAACTGACC	SHANK3 H22A(+1716+1733) 1mm_1	18mer
943	GGTGAAGCGTAACTGACC	SHANK3 H22A(+1716+1733) 1mm_10	18mer
944	GGTGAAGCGGAATTGACC	SHANK3 H22A(+1716+1733) 1mm_13	18mer
945	GGTGAAGCGGAACTTACC	SHANK3 H22A(+1716+1733) 1mm_15	18mer
946	GGTGAAGCGGAACTGATC	SHANK3 H22A(+1716+1733) 1mm_17	18mer
947	GGTGAAGCGGAACTGACT	SHANK3 H22A(+1716+1733) 1mm_18	18mer
948	GTTGAAGCGGAACTGACC	SHANK3 H22A(+1716+1733) 1mm_2	18mer
949	GGTGAAGCGGAACTGACC	SHANK3 H22A(+1716+1733) 1mm_4	18mer
950	GGTGAATCGGAACTGACC	SHANK3 H22A(+1716+1733) 1mm_7	18mer
951	GGTGAAGTGGAAGTACCCT	SHANK3 H22A(+1716+1733) 1mm_8	18mer
952	GGTGAAGCTGAACTGACC	SHANK3 H22A(+1716+1733) 1mm_9	18mer
953	GGTGAAGCGGAACTAACC	SHANK3 H22A(+1716+1733) mm1	18mer
954	AGGTGAAGCGGAACTGAC	SHANK3 H22A(+1717+1734)	18mer
955	AGGTGAAGCTGAACTGAC	SHANK3 H22A(+1717+1734) 1mm_10	18mer
956	AGGTGAAGCGTAACTGAC	SHANK3 H22A(+1717+1734) 1mm_11	18mer
957	AGGTGAAGCGGAATTGAC	SHANK3 H22A(+1717+1734) 1mm_14	18mer
958	AGGTGAAGCGGAACTTAC	SHANK3 H22A(+1717+1734) 1mm_16	18mer

959	AGGTGAAGCGGAACTGAT	SHANK3 H22A(+1717+1734) 1mm_18	18mer
960	ATGTGAAGCGGAACTGAC	SHANK3 H22A(+1717+1734) 1mm_2	18mer
961	AGTTGAAGCGGAACTGAC	SHANK3 H22A(+1717+1734) 1mm_3	18mer
962	AGGTGAAGCGGAACTGAC	SHANK3 H22A(+1717+1734) 1mm_5	18mer
963	AGGTGAATCGGAACTGAC	SHANK3 H22A(+1717+1734) 1mm_8	18mer
964	AGGTGAAGTGGAACTGAC	SHANK3 H22A(+1717+1734) 1mm_9	18mer
965	AGGTGAAGCGGAACTAAC	SHANK3 H22A(+1717+1734) mm1	18mer
966	GAGGTGAAGCGGAACTGA	SHANK3 H22A(+1718+1735)	18mer
967	TAGGTGAAGCGGAACTGA	SHANK3 H22A(+1718+1735) 1mm_1	18mer
968	GAGGTGAAGTGGAACTGA	SHANK3 H22A(+1718+1735) 1mm_10	18mer
969	GAGGTGAAGCTGAACTGA	SHANK3 H22A(+1718+1735) 1mm_11	18mer
970	GAGGTGAAGCGTAACTGA	SHANK3 H22A(+1718+1735) 1mm_12	18mer
971	GAGGTGAAGCGGAATTGA	SHANK3 H22A(+1718+1735) 1mm_15	18mer
972	GAGGTGAAGCGGAACTTA	SHANK3 H22A(+1718+1735) 1mm_17	18mer
973	GATGTGAAGCGGAACTGA	SHANK3 H22A(+1718+1735) 1mm_3	18mer
974	GAGTTGAAGCGGAACTGA	SHANK3 H22A(+1718+1735) 1mm_4	18mer
975	GAGGTGAAGCGGAACTGA	SHANK3 H22A(+1718+1735) 1mm_6	18mer
976	GAGGTGAATCGGAACTGA	SHANK3 H22A(+1718+1735) 1mm_9	18mer
977	GAGGTGAAGCGGAACTAA	SHANK3 H22A(+1718+1735) mm1	18mer
978	GGAGGTGAAGCGGAACTG	SHANK3 H22A(+1719+1736)	18mer
979	TGAGGTGAAGCGGAACTG	SHANK3 H22A(+1719+1736) 1mm_1	18mer
980	GGAGGTGAATCGGAACTG	SHANK3 H22A(+1719+1736) 1mm_10	18mer
981	GGAGGTGAAGTGGAACTG	SHANK3 H22A(+1719+1736) 1mm_11	18mer
982	GGAGGTGAAGCTGAACTG	SHANK3 H22A(+1719+1736) 1mm_12	18mer
983	GGAGGTGAAGCGTAACTG	SHANK3 H22A(+1719+1736) 1mm_13	18mer
984	GGAGGTGAAGCGGAATTG	SHANK3 H22A(+1719+1736) 1mm_16	18mer
985	GGAGGTGAAGCGGAACTT	SHANK3 H22A(+1719+1736) 1mm_18	18mer
986	GTAGGTGAAGCGGAACTG	SHANK3 H22A(+1719+1736) 1mm_2	18mer
987	GGATGTGAAGCGGAACTG	SHANK3 H22A(+1719+1736) 1mm_4	18mer
988	GGAGTTGAAGCGGAACTG	SHANK3 H22A(+1719+1736) 1mm_5	18mer
989	GGAGGTGAAGCGGAACTG	SHANK3 H22A(+1719+1736) 1mm_7	18mer
990	GGAGGTGAAGCGGAACTA	SHANK3 H22A(+1719+1736) mm1	18mer
991	AGGAGGTGAAGCGGAACT	SHANK3 H22A(+1720+1737)	18mer
992	AGGAGGTGAATCGGAACT	SHANK3 H22A(+1720+1737) 1mm_11	18mer
993	AGGAGGTGAAGTGGAACT	SHANK3 H22A(+1720+1737) 1mm_12	18mer
994	AGGAGGTGAAGCTGAACT	SHANK3 H22A(+1720+1737) 1mm_13	18mer
995	AGGAGGTGAAGCGTAACT	SHANK3 H22A(+1720+1737) 1mm_14	18mer
996	AGGAGGTGAAGCGGAATT	SHANK3 H22A(+1720+1737) 1mm_17	18mer
997	ATGAGGTGAAGCGGAACT	SHANK3 H22A(+1720+1737) 1mm_2	18mer
998	AGTAGGTGAAGCGGAACT	SHANK3 H22A(+1720+1737) 1mm_3	18mer
999	AGGATGTGAAGCGGAACT	SHANK3 H22A(+1720+1737) 1mm_5	18mer

1000	AGGAGTTGAAGCGGAACT	SHANK3 H22A(+1720+1737) 1mm_6	18mer
1001	AGGAGGTTAAGCGGAACT	SHANK3 H22A(+1720+1737) 1mm_8	18mer
1002	AGGAGGTGAAGCGAAACT	SHANK3 H22A(+1720+1737) mm1	18mer
1003	AAGGAGGTGAAGCGGAAC	SHANK3 H22A(+1721+1738)	18mer
1004	AAGGAGGTGAATCGGAAC	SHANK3 H22A(+1721+1738) 1mm_12	18mer
1005	AAGGAGGTGAAGTGAAC	SHANK3 H22A(+1721+1738) 1mm_13	18mer
1006	AAGGAGGTGAAGCTGAAC	SHANK3 H22A(+1721+1738) 1mm_14	18mer
1007	AAGGAGGTGAAGCGTAAC	SHANK3 H22A(+1721+1738) 1mm_15	18mer
1008	AAGGAGGTGAAGCGGAAT	SHANK3 H22A(+1721+1738) 1mm_18	18mer
1009	AATGAGGTGAAGCGGAAC	SHANK3 H22A(+1721+1738) 1mm_3	18mer
1010	AAGTAGGTGAAGCGGAAC	SHANK3 H22A(+1721+1738) 1mm_4	18mer
1011	AAGGATGTGAAGCGGAAC	SHANK3 H22A(+1721+1738) 1mm_6	18mer
1012	AAGGAGTTGAAGCGGAAC	SHANK3 H22A(+1721+1738) 1mm_7	18mer
1013	AAGGAGGTTAAGCGGAAC	SHANK3 H22A(+1721+1738) 1mm_9	18mer
1014	AAGGAGGTGAAGCGAAAC	SHANK3 H22A(+1721+1738) mm1	18mer
1015	AAAGGAGGTGAAGCGGAA	SHANK3 H22A(+1722+1739)	18mer
1016	AAAGGAGGTTAAGCGGAA	SHANK3 H22A(+1722+1739) 1mm_10	18mer
1017	AAAGGAGGTGAATCGGAA	SHANK3 H22A(+1722+1739) 1mm_13	18mer
1018	AAAGGAGGTGAAGTGGAA	SHANK3 H22A(+1722+1739) 1mm_14	18mer
1019	AAAGGAGGTGAAGCTGAA	SHANK3 H22A(+1722+1739) 1mm_15	18mer
1020	AAAGGAGGTGAAGCGTAA	SHANK3 H22A(+1722+1739) 1mm_16	18mer
1021	AAATGAGGTGAAGCGGAA	SHANK3 H22A(+1722+1739) 1mm_4	18mer
1022	AAAGTAGGTGAAGCGGAA	SHANK3 H22A(+1722+1739) 1mm_5	18mer
1023	AAAGGATGTGAAGCGGAA	SHANK3 H22A(+1722+1739) 1mm_7	18mer
1024	AAAGGAGTTGAAGCGGAA	SHANK3 H22A(+1722+1739) 1mm_8	18mer
1025	AAAGGAGGTGAAGCGAAA	SHANK3 H22A(+1722+1739) mm1	18mer
1026	AAAAGGAGGTGAAGCGGA	SHANK3 H22A(+1723+1740)	18mer
1027	AAAAGGAGGTTAAGCGGA	SHANK3 H22A(+1723+1740) 1mm_11	18mer
1028	AAAAGGAGGTGAATCGGA	SHANK3 H22A(+1723+1740) 1mm_14	18mer
1029	AAAAGGAGGTGAAGTGA	SHANK3 H22A(+1723+1740) 1mm_15	18mer
1030	AAAAGGAGGTGAAGCTGA	SHANK3 H22A(+1723+1740) 1mm_16	18mer
1031	AAAAGGAGGTGAAGCGTA	SHANK3 H22A(+1723+1740) 1mm_17	18mer
1032	AAAATGAGGTGAAGCGGA	SHANK3 H22A(+1723+1740) 1mm_5	18mer
1033	AAAAGTAGGTGAAGCGGA	SHANK3 H22A(+1723+1740) 1mm_6	18mer
1034	AAAAGGATGTGAAGCGGA	SHANK3 H22A(+1723+1740) 1mm_8	18mer
1035	AAAAGGAGTTGAAGCGGA	SHANK3 H22A(+1723+1740) 1mm_9	18mer
1036	AAAAGGAGGTGAAGCGAA	SHANK3 H22A(+1723+1740) mm1	18mer
1037	CAAAAGGAGGTGAAGCGG	SHANK3 H22A(+1724+1741)	18mer
1038	TAAAAGGAGGTGAAGCGG	SHANK3 H22A(+1724+1741) 1mm_1	18mer
1039	CAAAAGGAGTTGAAGCGG	SHANK3 H22A(+1724+1741) 1mm_10	18mer
1040	CAAAAGGAGGTTAAGCGG	SHANK3 H22A(+1724+1741) 1mm_12	18mer

1041	CAAAAGGAGGTGAATCGG	SHANK3 H22A(+1724+1741) 1mm_15	18mer
1042	CAAAAGGAGGTGAAGTGG	SHANK3 H22A(+1724+1741) 1mm_16	18mer
1043	CAAAAGGAGGTGAAGCTG	SHANK3 H22A(+1724+1741) 1mm_17	18mer
1044	CAAAAGGAGGTGAAGCGT	SHANK3 H22A(+1724+1741) 1mm_18	18mer
1045	CAAAATGAGGTGAAGCGG	SHANK3 H22A(+1724+1741) 1mm_6	18mer
1046	CAAAAGTAGGTGAAGCGG	SHANK3 H22A(+1724+1741) 1mm_7	18mer
1047	CAAAAGGATGTGAAGCGG	SHANK3 H22A(+1724+1741) 1mm_9	18mer
1048	CAAAAGGAGGTGAAGCGA	SHANK3 H22A(+1724+1741) mm1	18mer
1049	ACAAAAGGAGGTGAAGCG	SHANK3 H22A(+1725+1742)	18mer
1050	ACAAAAGGATGTGAAGCG	SHANK3 H22A(+1725+1742) 1mm_10	18mer
1051	ACAAAAGGAGTTGAAGCG	SHANK3 H22A(+1725+1742) 1mm_11	18mer
1052	ACAAAAGGAGGTGAAGCG	SHANK3 H22A(+1725+1742) 1mm_13	18mer
1053	ACAAAAGGAGGTGAATCG	SHANK3 H22A(+1725+1742) 1mm_16	18mer
1054	ACAAAAGGAGGTGAAGTG	SHANK3 H22A(+1725+1742) 1mm_17	18mer
1055	ACAAAAGGAGGTGAAGCT	SHANK3 H22A(+1725+1742) 1mm_18	18mer
1056	ATAAAAGGAGGTGAAGCG	SHANK3 H22A(+1725+1742) 1mm_2	18mer
1057	ACAAAATGAGGTGAAGCG	SHANK3 H22A(+1725+1742) 1mm_7	18mer
1058	ACAAAAGTAGGTGAAGCG	SHANK3 H22A(+1725+1742) 1mm_8	18mer
1059	ACAAAAGGAGGTGAAGCA	SHANK3 H22A(+1725+1742) mm1	18mer
1060	TACAAAAGGAGGTGAAGC	SHANK3 H22A(+1726+1743)	18mer
1061	TACAAAAGGATGTGAAGC	SHANK3 H22A(+1726+1743) 1mm_11	18mer
1062	TACAAAAGGAGTTGAAGC	SHANK3 H22A(+1726+1743) 1mm_12	18mer
1063	TACAAAAGGAGGTGAAGC	SHANK3 H22A(+1726+1743) 1mm_14	18mer
1064	TACAAAAGGAGGTGAATC	SHANK3 H22A(+1726+1743) 1mm_17	18mer
1065	TACAAAAGGAGGTGAAGT	SHANK3 H22A(+1726+1743) 1mm_18	18mer
1066	TATAAAAGGAGGTGAAGC	SHANK3 H22A(+1726+1743) 1mm_3	18mer
1067	TACAAAATGAGGTGAAGC	SHANK3 H22A(+1726+1743) 1mm_8	18mer
1068	TACAAAAGTAGGTGAAGC	SHANK3 H22A(+1726+1743) 1mm_9	18mer
1069	TACAAAAGGAGGTGAAAC	SHANK3 H22A(+1726+1743) mm1	18mer
1070	ATACAAAAGGAGGTGAAG	SHANK3 H22A(+1727+1744)	18mer
1071	ATACAAAAGTAGGTGAAG	SHANK3 H22A(+1727+1744) 1mm_10	18mer
1072	ATACAAAAGGATGTGAAG	SHANK3 H22A(+1727+1744) 1mm_12	18mer
1073	ATACAAAAGGAGTTGAAG	SHANK3 H22A(+1727+1744) 1mm_13	18mer
1074	ATACAAAAGGAGGTGAAG	SHANK3 H22A(+1727+1744) 1mm_15	18mer
1075	ATACAAAAGGAGGTGAAT	SHANK3 H22A(+1727+1744) 1mm_18	18mer
1076	ATATAAAAGGAGGTGAAG	SHANK3 H22A(+1727+1744) 1mm_4	18mer
1077	ATACAAAATGAGGTGAAG	SHANK3 H22A(+1727+1744) 1mm_9	18mer
1078	ATACAAAAGGAGGTGAAA	SHANK3 H22A(+1727+1744) mm1	18mer

Table 2: Exemplary length-matured ASOs targeting a region (SEQ ID NO:1079) of the 3' UTR of SHANK3

SEQ ID NO.	ASO Sequence	ASO Name	ASO length
1080	ACTGACCCTGTAAAGTTAAA	SHANK3_H22A(+1703+1722)	20mer
1081	GAAGTACCCTGTAAAGTTA	SHANK3_H22A(+1705+1724)	20mer
1082	CGGAAGTACCCTGTAAAGT	SHANK3_H22A(+1707+1726)	20mer
1083	ACTGACCCTGTAAAGT	SHANK3_H22A(+1707+1722)	16mer
1084	AACTGACCCTGTAAA	SHANK3_H22A(+1709+1723)	15mer
1085	ACCCTGTAAAGTTAAAAA	SHANK3_H22A(+1701+1718)	18mer
1086	TGACCCTGTAAAGTTAAAAA	SHANK3_H22A(+1701+1720)	20mer
1087	AGCGGAAGTACCCTGTAAA	SHANK3_H22A(+1709+1728)	20mer
1088	AAGCGGAAGTACCCTGTAA	SHANK3_H22A(+1710+1729)	20mer
1089	CATACAAAAGGAGGTGAA	SHANK3_H22A(+1728+1745)	18mer
1090	TCCATACAAAAGGAGGTGAA	SHANK3_H22A(+1728+1747)	20mer
1091	ATGGAACTCCATACAAAA	SHANK3_H22A(+1737+1754)	18mer
1092	AATTGAACGGAACCAAAA	SHANK3_H22A(+1679+1696)	18mer
1093	TAAAGTTAAAAACCCAAA	SHANK3_H22A(+1695+1712)	18mer
1094	GCGGAAGTACCCTGTAA	SHANK3_H22A(+1711+1727)	17mer
1095	CGGAAGTACCCTGTAAAGTTAAAA	SHANK3_H22A(+1702+1726)	25mer

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Table 3: Exemplary chemistry-matured ASOs a region (SEQ ID NO:1079) of the 3' UTR of SHANK3

(Note: LNA modified nucleotides are denoted by a "*" and abasic spacers with an "S".)

SEQ ID NO.	ASO Sequence	ASO Name	ASO length
1096	AACT*GACC*CTGT*AAA	SHANK3_H22A(+1709+1723) 3lna 4 8 12	15mer
1097	AACT*GAC*CCTGT*AAA	SHANK3_H22A(+1709+1723) 3lna 4 7 12	15mer
1098	AACT*GACCCTGT*AAA	SHANK3_H22A(+1709+1723) 2lna 4 12	15mer
1099	AACTGAC*CCTGT*AAA	SHANK3_H22A(+1709+1723) 2lna 7 12	15mer
1100	AACTGA*CCCTGT*AAA	SHANK3_H22A(+1709+1723) 2lna 6 12	15mer
1101	A*ACTGACCCT*GTAAA	SHANK3_H22A(+1709+1723) 2lna 1 10	15mer
1102	AACTGA*CCCTGTAAA*	SHANK3_H22A(+1709+1723) 2lna 6 15	15mer
1103	A*ACTGACC*CTGTAAA*	SHANK3_H22A(+1709+1723) 3lna 1 8 15	15mer
1104	AGCG*SA*ACTGACCCTGTAAA	SHANK3_H22A(+1709+1728) 1spr 5 2lna 4 6	20mer
1105	AGCG*SA*ACTGACSCCTGTAAA	SHANK3_H22A(+1709+1728) 2spr 5 13 2lna 4 6	20mer
1106	AGCGGAAGT*SA*CCCTGTAAA	SHANK3_H22A(+1709+1728) 1spr 10 2lna 9 11	20mer
1107	AGC*GGAAGTACCCTGT*AAA	SHANK3_H22A(+1709+1728) 2lna 3 17	20mer
1108	AGCG*SAAGTACCCTGT*AAA	SHANK3_H22A(+1709+1728) 1spr 5 2lna 4 17	20mer
1109	GCG*SA*ACTGACCCTGTAA	SHANK3_H22A(+1711+1727) 1spr 4 2lna 3 5	17mer
1110	GCGGAAGT*SA*CCCTGTAA	SHANK3_H22A(+1711+1727) 1spr 9 2lna 8 10	17mer
1111	GCGGA*ACTGA*CCCT*GTAA	SHANK3_H22A(+1711+1727) 3lna 5 10 14	17mer

1112	GC*GGAAGTACCCTGT*A	SHANK3_H22A(+1711+1727)_2lna_2_16	17mer
1113	GC*SGAAGTACCCTGT*A	SHANK3_H22A(+1711+1727)_1spr_3_2lna_2_16	17mer
1114	ATG*SA*ACTCCATACAAAA	SHANK3_H22A(+1737+1754)_1spr_4_2lna_3_5	18mer
1115	ATG*SA*ACTCCATASAAAA	SHANK3_H22A(+1737+1754)_2spr_4_14_2lna_3_5	18mer
1116	ATG*SA*ACTCSATACAAAA	SHANK3_H22A(+1737+1754)_2spr_4_10_2lna_3_5	18mer
1117	ATGGAACTC*SA*TACAAAA	SHANK3_H22A(+1737+1754)_1spr_10_2lna_9_11	18mer
1118	ATGGAACTCCATA*SA*AAA	SHANK3_H22A(+1737+1754)_1spr_14_2lna_13_15	18mer
1119	AT*GGAAGTCCATACAA*AA	SHANK3_H22A(+1737+1754)_2lna_2_16	18mer
1120	ATG*GAAGTCCATACAA*AA	SHANK3_H22A(+1737+1754)_2lna_3_16	18mer
1121	TAAAGTTAAAAAC*SC*AAA	SHANK3_H22A(+1695+1712)_1spr_14_2lna_13_15	18mer
1122	TAA*SG*TTAAAAACCCAAA	SHANK3_H22A(+1695+1712)_1spr_4_2lna_3_5	18mer
1123	TAA*SG*TTAAAAACSCAAA	SHANK3_H22A(+1695+1712)_2spr_4_14_2lna_3_5	18mer
1124	TAAAGTTAA*SA*ACCCAAA	SHANK3_H22A(+1695+1712)_1spr_10_2lna_9_11	18mer
1125	TAA*AGTT*AAAAACCCA*AA	SHANK3_H22A(+1695+1712)_3lna_3_7_16	18mer
1126	AATTGAA*SG*GAACCAAAA	SHANK3_H22A(+1679+1696)_1spr_8_2lna_7_9	18mer
1127	AATTGAACG*SA*ACCAAAA	SHANK3_H22A(+1679+1696)_1spr_10_2lna_9_11	18mer
1128	AATTGAACGGAA*SC*AAAA	SHANK3_H22A(+1679+1696)_1spr_13_2lna_12_14	18mer
1129	AATTG*SA*CGGAACCAAAA	SHANK3_H22A(+1679+1696)_1spr_6_2lna_5_7	18mer
1130	AATTSACG*SA*ACCAAAA	SHANK3_H22A(+1679+1696)_2spr_5_10_2lna_9_11	18mer
1131	AATTG*SA*CGGAASCAAAA	SHANK3_H22A(+1679+1696)_2spr_6_13_2lna_5_7	18mer
1132	AA*TTGAACGGA*ACCAAAA	SHANK3_H22A(+1679+1696)_2lna_2_11	18mer
1133	AA*TTGAACGSA*ACCAAAA	SHANK3_H22A(+1679+1696)_1spr_10_2lna_2_11	18mer

CLAIMS:

1. An antisense oligonucleotide (ASO) that binds within a targeted portion of the 3' UTR of a *SHANK3* mRNA;
whereby binding of the antisense oligonucleotide within the targeted portion in a mammalian cell results in an increased level of SHANK3 protein in the mammalian cell.
2. A vector for expression, in a mammalian cell, of an antisense RNA (AR) that binds within a targeted portion of the 3' UTR of a *SHANK3* mRNA;
whereby binding of the AR within the targeted portion in a mammalian cell results in an increased level of SHANK3 protein in the mammalian cell.
3. The ASO according to claim 1 or the vector according to claim 2, wherein the mammalian cell is a neuron.
4. The vector according to claim 3, wherein the vector comprises a neuron-selective promoter for driving expression of the antisense RNA in the mammalian neuron.
5. The vector according to claim 4, wherein the neuron-selective promoter is selective for expression in a neuron type selected from the list consisting of: cortical, striatal, cerebellar and hippocampal excitatory or inhibitory neurons, including, but not limited to cortical glutamatergic neurons, cortical GABAergic neurons, hippocampal glutamatergic neurons, and striatal inhibitory neurons.
6. The vector according to any one of claims 2 to 5, wherein the vector comprises an inducible promoter.
7. The vector according to any one of claims 2 to 6, wherein the vector is a viral vector.

8. The vector according to claim 7, wherein the viral vector is a recombinant virus selected from the group consisting of: adeno-associated virus (AAV), adenovirus, lentivirus, and anellovirus.
9. The vector according to any one of claims 2 to 8, wherein the vector is a non-viral vector.
10. The non-viral vector according to claim 9, further comprising a transfection agent.
11. The ASO or vector according to any one of claims 1 to 10, wherein the sequence of the ASO or AR comprises up to two base mismatches to the targeted portion.
12. The ASO according to any one of claims 1, 3, or 11, wherein the ASO comprises a backbone modification.
13. The method or ASO according to claim 12, wherein the ASO comprises a backbone modification comprising a phosphorothioate linkage or a phosphorodiamidate linkage.
14. The ASO according to claim 12 or claim 13, wherein the ASO comprises a phosphorodiamidate morpholino, a locked nucleic acid, a peptide nucleic acid, an arabinonucleic acid, a 2'-O-methyl, a 2'-fluoro, a 2'-O-methoxyethyl moiety, or an abasic spacer subunit.
15. The ASO according to any one of claims 12 to 14, wherein the ASO comprises at least one modified sugar moiety.
16. The ASO according to claim 15, wherein each sugar moiety in the ASO is a modified sugar moiety.

17. The ASO according to any one of claims 12 to 16, wherein the ASO comprises a 2'-*O*-methoxyethyl moiety.
18. The ASO according to claim 17, wherein each nucleotide of the ASO comprises a 2'-*O*-methoxyethyl moiety.
19. The ASO according to any one of claims 1, 3, or 11 to 18, or the vector according to any one of claims 2 to 11, wherein the nucleotide sequence of the ASO or the AR consists of 10 to 50 nucleotides, 15 to 40 nucleotides, 18 to 40 nucleotides, 17 to 25 nucleotides, 20 to 35 nucleotides, 15 to 30 nucleotides, 20 to 30 nucleotides, 22 to 30 nucleotides, 24 to 30 nucleotides, 25 to 30 nucleotides, or 26 to 30 nucleotides.
20. The ASO according to claim 19, wherein the nucleotide sequence of the ASO or the AR consists of 15 to 30 nucleotides.
21. The ASO according to claim 20, wherein the ASO comprises one or more phosphorodiamidate morpholino moieties.
22. The ASO according to any one of claims 1, 3, or 11 to 21, wherein the ASO is linked to a functional moiety.
23. The ASO according to claim 22, wherein the functional moiety comprises a delivery moiety.
24. The ASO according to claim 23, wherein the delivery moiety is selected from the group consisting of lipids, polyethers, peptides, carbohydrates, receptor binding peptide (RBP), and antibodies.
25. The ASO according to claim 23 or claim 24, wherein the delivery moiety comprises a cell-penetrating peptide (CPP).

26. The ASO according to claim 23 or claim 24, wherein the delivery moiety comprises a *N*-acetylgalactosamine (GalNAc) moiety or a glycan moiety.
27. The ASO according to any one of claims 23 to 25, wherein the delivery moiety comprises a fatty acid or lipid moiety.
28. The ASO according to claim 27, wherein the fatty acid chain length is about C8 to C20.
29. The ASO according to claim 23, wherein the functional moiety comprises a stabilising moiety.
30. The ASO according to any one of claims 23 to 29, wherein the functional moiety is covalently linked to the ASO.
31. The ASO according to any one of claims 23 to 29, wherein the functional moiety is non-covalently linked to the ASO.
32. The ASO according to any one of claims 23 to 31, wherein the functional moiety is linked to the 5' end of the ASO.
33. The ASO according to any one of claims 23 to 31, wherein the functional moiety is linked to the 3' end of the ASO.
34. The ASO or vector according to any one of claims 1 to 33, wherein the nucleotide sequence of the ASO or the AR is at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% complementary to the nucleotide sequence of the targeted portion over the length of the ASO or the AR.
35. The ASO or vector according to any one of claims 1 to 34, wherein the targeted portion comprises the sequence corresponding to **SEQ ID NO:1079**.

36. The ASO or vector according to claim 35, wherein the sequence of the targeted portion consists of the sequence corresponding to **SEQ ID NO:1079**.
37. The vector according to any one of claims 2 to 11, 35 or 36, wherein the nucleotide sequence of the AR corresponds to any one of **SEQ ID NOs:1080-1093**.
38. The ASO according to any one of claims 1 or 11 to 36, wherein the nucleotide sequence of the ASO comprises an abasic spacer subunit or a locked nucleic acid.
39. The ASO according to claim 38, wherein the nucleotide sequence of the ASO comprises an abasic spacer subunit and a locked nucleic acid.
40. The ASO according to any one of claims 1 or 11 to 36, wherein the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1080-1093** or **1096-1133**.
41. The ASO according to claim 40, wherein the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1080-1093**.
42. The ASO according to claim 41, wherein the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1084, 1087, or 1091-1093**.
43. The ASO according to claim 40, wherein the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1096-1133**.
44. The ASO according to claim 43, wherein the nucleotide sequence of the ASO corresponds to any one of **SEQ ID NOs:1096, 1109, 1119, and 1128**.
45. The ASO according to any one of claims 1 or 11 to 44, further comprising a delivery nanocarrier, wherein the nanocarrier is complexed with the ASO.

46. The ASO according to claim 45, wherein the delivery nanocarrier is selected from the group consisting of: lipoplexes, liposomes, exosomes, inorganic nanoparticles, and DNA nanostructures.
47. The ASO according to claim 46, wherein the delivery nanocarrier comprises a lipid nanoparticle (LNP) encapsulating the ASO.
48. A pharmaceutical composition comprising the ASO, vector, or composition according to any one of claims 1 to 47, and a pharmaceutically acceptable excipient.
49. The pharmaceutical composition according to claim 48, wherein the pharmaceutical composition comprises the ASO.
50. The pharmaceutical composition according to claim 49, wherein the pharmaceutical composition is provided as a lyophilic formulation of the ASO.
51. A method for preventing or treating a condition associated with SHANK3 haploinsufficiency, the method comprising administering to a subject in need thereof a therapeutically effective amount of the pharmaceutical composition according to any one of claims 48 to 50.
52. The method according to claim 51, wherein the condition is Phelan-McDermid syndrome, an autism spectrum disorder, schizophrenia, or an intellectual disability.
53. The method according to claim 51 or claim 52, wherein the condition is Phelan-McDermid syndrome.
54. The method according to any one of claims 51 to 53, wherein the subject is a human subject.

55. Use of the ASO or vector according to any one of claims 1 to 47 in the manufacture of a medicament for prevention or treatment of a condition associated with SHANK3 haploinsufficiency.
56. The method according to any one of claims 51 to 54, or the use according to claim 55, wherein the level of SHANK3 protein in at least a plurality of cells in the subject is increased about 1.1 to about 5 fold in cells, *e.g.*, 1.2 fold, 1.3 fold, 1.5 fold, 1.7 fold, 2 fold, 2.2 fold, 2.5 fold, 2.7 fold, 3 fold, 3.3 fold, 3.5 fold, 4 fold, 4.3 fold, 4.5 fold, 4.7 fold, or another increase in SHANK3 protein levels from about 1.1 fold to about 5 fold compared to the level in the absence of the pharmaceutical composition.
57. A genetically modified cell comprising the ASO or vector according to any one of claims 1 to 47.
58. The genetically modified cell according to claim 57, wherein the genetically modified cell is a mammalian cell.
59. The genetically modified mammalian cell according to claim 58, wherein the genetically modified mammalian cell is a human cell.
60. The genetically modified mammalian cell according to claim 58 or claim 59, wherein the genetically modified mammalian cell is a genetically modified neuron or neural progenitor.
61. The genetically modified mammalian neuron according to claim 60, wherein the genetically modified mammalian neuron is a neuron selected from the group consisting of: cortical, striatal, cerebellar and hippocampal excitatory or inhibitory neurons, cortical glutamatergic neurons, cortical GABAergic neurons, hippocampal glutamatergic neurons, and striatal inhibitory neurons.

62. The genetically modified mammalian neuron according to claim 60 or claim 61, wherein the genetically modified mammalian cell is a cortical glutamatergic neuron obtained by differentiation of an hiPSC line, wherein the hiPSC line is derived from a subject suffering from Phelan-McDermid syndrome or a subject not suffering from Phelan-McDermid syndrome.
63. The genetically modified mammalian cell according to any one of claims 58 to 62, wherein the genetically modified mammalian cell is from a cell line.
64. The genetically modified mammalian cell according to claim 63, wherein the cell line is a hiPSC cell line or a cell line derived from neurons.