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**Treatment Of Muscle Disorder With Folliculin Interacting Protein 1 (FNIP1) Inhibitors And/Or
Folliculin (FLCN) Inhibitors**

Reference To Sequence Listing

5 This application includes a Sequence Listing filed electronically as an XML file named 381204286SEQ, created on August 21, 2024, with a size of 106,382 bytes. The Sequence Listing is incorporated herein by reference.

Field

10 The present disclosure generally relates to the treatment of subjects having muscle disorder or at risk of developing muscle disorder by administering a Folliculin Interacting Protein 1 (FNIP1) inhibitor and/or a Folliculin (FLCN) inhibitor to the subject, and to methods of identifying subjects having an increased risk of developing muscle disorder.

15 **Background**

 Causes of muscle disorders include: injury or overuse, such as sprains or strains, cramps or tendinitis; a genetic disorder, such as muscular dystrophy; some cancers; inflammation, such as myositis, diseases of nerves that affect muscles; infections; and certain medicines. Muscle disorders include sarcopenia, Duchenne Muscular Dystrophy, and Pompe
20 disease.

 Folliculin (FLCN) is encoded by a 25 kb gene located at 17p11.2. FLCN is 579 amino acids long and is a 64 kDa multi-functional protein involved in both the cellular response to amino acid availability and in the regulation of glycolysis. Specifically, FLCN regulates the mTORC1 signaling cascade controlling the MIT/TFE factors TFEB and TFE3 in the cellular
25 response to amino acid availability and regulates glycolysis by binding to lactate dehydrogenase LDHA, acting as an uncompetitive inhibitor. In addition, FLCN activates mTORC1 by acting as a GTPase-activating protein by stimulating GTP hydrolysis by RRAGC/RagC or RRAGD/RagD, promoting the conversion to the GDP-bound state of RRAGC/RagC or RRAGD/RagD, and thereby activating the kinase activity of mTORC1.

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Folliculin Interacting Protein 1 (FNIP1) is encoded by a 155 kb gene located at 5q31.1. FNIP1 is 1166 amino acids long and is a 130 kDa protein that participates in the regulation of cellular metabolism and nutrient sensing by modulating the AMP-activated protein Kinase (AMPK) and target of rapamycin signaling pathways. In addition, FNIP1 binds to the tumor suppressor protein folliculin as well as associates with the molecular chaperone heat shock protein-90 (Hsp90) and negatively regulates its ATPase activity by facilitating its association with folliculin.

Summary

10 The present disclosure provides methods of treating a subject having muscle disorder or at risk of developing muscle disorder, the methods comprising administering an FNIP1 inhibitor and/or an FLCN inhibitor to the subject.

 The present disclosure also provides methods of treating a subject having muscle disorder or at risk of developing muscle disorder by administering a muscle disorder
15 therapeutic agent, the methods comprising: determining or having determined whether the subject has an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, by: obtaining or having obtained a biological sample from the subject; and performing or having performed a sequence analysis on the biological sample to determine if the subject has a genotype comprising an FNIP1 variant nucleic acid molecule and/or an FLCN
20 variant nucleic acid molecule; and administering or continuing to administer the muscle disorder therapeutic agent in a standard dosage amount, and/or administering an FNIP1 inhibitor and/or an FLCN inhibitor to a subject that is FNIP1 reference and/or FLCN reference; administering or continuing to administer the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and/or administering an FNIP1
25 inhibitor and/or an FLCN inhibitor to a subject that is heterozygous for the FNIP1 variant nucleic acid molecule and/or the FLCN variant nucleic acid molecule; or administering or continuing to administer the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount to a subject that is homozygous for the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule; wherein the presence the FNIP1 variant
30 nucleic acid molecule and/or the FLCN variant nucleic acid molecule indicates the subject has a decreased risk of developing muscle disorder.

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The present disclosure also provides methods of identifying a subject having an increased risk of developing muscle disorder, the methods comprising: determining or having determined the presence or absence of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule in a biological sample obtained from the subject; wherein: when
5 the subject is FNIP1 reference and/or FLCN reference, then the subject has an increased risk of developing muscle disorder; and when the subject is heterozygous or homozygous for the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, then the subject has a decreased risk of developing muscle disorder.

The present disclosure also provides muscle disorder therapeutic agents for use in the
10 treatment or prevention of muscle disorder in a subject having an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule.

The present disclosure also provides FNIP1 inhibitors for use in the treatment or prevention of muscle disorder in a subject that is FNIP1 reference or is heterozygous for an FNIP1 variant nucleic acid molecule.

15 The present disclosure also provides FLCN inhibitors for use in the treatment or prevention of muscle disorder in a subject that is FLCN reference or is heterozygous for an FLCN variant nucleic acid molecule.

Brief Description Of The Drawings

20 The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Figure 1 shows identification of FNIP1 rare coding variation associated with blood lipids and liver enzymes in ExWAS; the largest effect was observed with lower triglycerides and
25 ALT.

Figure 2 shows identification of genome-wide association analysis with a common missense (5:131672501:T:C--Gln648Arg) variant in FNIP1 to be associated with TGL:HDL ratio.

Figure 3 shows association of FNIP1 rare coding variants with higher HDLC and lower triglycerides and LDLC levels; FLCN shows similar pattern of associations.

30 Figure 4 shows association of FNIP1 and FLCN rare coding variants with lower ALT levels; FLCN pLoFs are associated with lower MRI derived liver fat and inflammation.

Figure 5 shows the impact of FNIP1 and FLCN rare coding variants on ALT and PDFF.

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Figure 6 shows association of FNIP1 rare coding variants with lower odds for NALD.

Figure 7 shows association of common FNIP1 missense variant with liver enzymes.

Figure 8 shows association of FNIP1 and FLCN rare coding variants with lower waist to hip ratio and body fat percentage.

5 Figure 9 shows the impact of rare variation in FNIP1 on body fat distribution.

Figure 10 shows association of FNIP1 and FLCN rare coding variants with lower HbA1c levels and lower odds of type 2 diabetes.

Figure 11 shows association of FNIP1 and FLCN rare coding variants with lower eGFR.

Figure 12 shows FNIP1 pLoF had general protective cardiometabolic associations.

10 Figure 13 shows FNIP1 pLoF had general protective cardiometabolic associations.

Figure 14 shows FNIP1 common missense variant phenome-wide associations are similar to FNIP1 rare coding associations.

Figure 15 shows FNIP1 common missense variant shows strongest association with lower odds for T2D.

15 Figure 16 shows FNIP1 or FLCN inhibition in skeletal muscle induced an increase in oxidative muscle fibers and mitochondrial gene expression; AAVmyo2A was obtained from SignaGen Laboratories (Catalog # SL100862).

Figure 17 shows FNIP1 or FLCN inhibition in skeletal muscle enhanced vascularization and muscle glycogen content.

20 Figure 18 shows FLCN inhibition in skeletal muscle induced an increase in oxidative muscle fibers, enhanced vascularity, and increased glycogen content.

Description

Various terms relating to aspects of the present disclosure are used throughout the specification and claims. Such terms are to be given their ordinary meaning in the art, unless
25 otherwise indicated. Other specifically defined terms are to be construed in a manner consistent with the definitions provided herein.

Unless otherwise expressly stated, it is in no way intended that any method or aspect set forth herein be construed as requiring that its steps be performed in a specific order. Accordingly, where a method claim does not specifically state in the claims or descriptions that
30 the steps are to be limited to a specific order, it is in no way intended that an order be inferred, in any respect. This holds for any possible non-expressed basis for interpretation, including matters of logic with respect to arrangement of steps or operational flow, plain meaning

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derived from grammatical organization or punctuation, or the number or type of aspects described in the specification.

As used herein, the singular forms “a,” “an” and “the” include plural referents unless the context clearly dictates otherwise.

5 As used herein, the term “about” means that the recited numerical value is approximate and small variations would not significantly affect the practice of the disclosed embodiments. Where a numerical value is used, unless indicated otherwise by the context, the term “about” means the numerical value can vary by $\pm 10\%$ and remain within the scope of the disclosed embodiments.

10 As used herein, the term “comprising” may be replaced with “consisting” or “consisting essentially of” in particular embodiments as desired.

 As used herein, the terms “nucleic acid”, “nucleic acid molecule”, “nucleic acid sequence”, “polynucleotide”, or “oligonucleotide” can comprise a polymeric form of nucleotides of any length, can comprise DNA and/or RNA, and can be single-stranded, double-
15 stranded, or multiple stranded. One strand of a nucleic acid also refers to its complement.

 As used herein, the term “subject” includes any animal, including mammals. Mammals include, but are not limited to, farm animals (such as, for example, horses, cows, and pigs), companion animals (such as, for example, dogs and cats), laboratory animals (such as, for example, mice, rats, and rabbits), and non-human primates. In some embodiments, the subject
20 is a human. In some embodiments, the human is a patient under the care of a physician.

 It has been observed in accordance with the present disclosure that rare FNIP1 variant nucleic acid molecule and rare FLCN variant nucleic acid molecules (whether these variants are homozygous or heterozygous in a particular subject) associate with a decreased risk of developing muscle disorder. It is believed that FNIP1 variant nucleic acid molecule and/or an
25 FLCN variant nucleic acid molecules have not been associated with muscle disorder in humans. Therefore, subjects that are FNIP1 reference and/or FLCN reference or heterozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule may be treated with an FNIP1 inhibitor and/or an FLCN inhibitor such that muscle disorder is inhibited or prevented, the symptoms thereof are reduced or prevented, and/or development of
30 symptoms is repressed or prevented. It is also believed that such subjects having muscle disorder may further be treated with one or more muscle disorder therapeutic agents. In addition, the present disclosure provides methods of leveraging the presence or absence of

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FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecules in subjects to identify or stratify risk is such subjects of developing muscle disorder, or to diagnose subjects as having an increased risk of developing muscle disorder.

For purposes of the present disclosure, any particular subject, such as a human, can be categorized as having one of three FNIP1 genotypes: i) FNIP1 reference; ii) heterozygous for an FNIP1 variant nucleic acid molecule ; or iii) homozygous for an FNIP1 variant nucleic acid molecule. A subject is FNIP1 reference when the subject does not have a copy of an FNIP1 variant nucleic acid molecule. A subject is heterozygous for an FNIP1 variant nucleic acid molecule when the subject has a single copy of an FNIP1 variant nucleic acid molecule. A subject is homozygous for an FNIP1 variant nucleic acid molecule when the subject has two copies of an FNIP1 variant nucleic acid molecule.

For purposes of the present disclosure, any particular subject, such as a human, can be categorized as having one of three FLCN genotypes: i) FLCN reference; ii) heterozygous for an FLCN variant nucleic acid molecule; or iii) homozygous for an FLCN variant nucleic acid molecule. A subject is FLCN reference when the subject does not have a copy of an FLCN variant nucleic acid molecule. A subject is heterozygous for an FLCN variant nucleic acid molecule when the subject has a single copy of an FLCN variant nucleic acid molecule. A subject is homozygous for an FLCN variant nucleic acid molecule when the subject has two copies of an FLCN variant nucleic acid molecule.

In any of the embodiments described herein, the FNIP1 variant nucleic acid molecule can be any nucleic acid molecule (such as, a genomic nucleic acid molecule, an mRNA molecule, or a cDNA molecule produced from an mRNA molecule) encoding an FNIP1 variant polypeptide having a partial loss-of-function, a complete loss-of-function, a predicted partial loss-of-function, or a predicted complete loss-of-function. A subject who has an FNIP1 polypeptide having a partial loss-of-function (or predicted partial loss-of-function) is hypomorphic for FNIP1. In some embodiments, the FNIP1 variant nucleic acid molecule results in decreased or aberrant expression or activity of FNIP1 mRNA or polypeptide. In some embodiments, the FNIP1 variant nucleic acid molecule is associated with a reduced *in vitro* response to FNIP1 ligands compared with reference FNIP1. In some embodiments, the FNIP1 variant nucleic acid molecule is a splice-site variant, a stop-gain variant, a start-loss variant, a stop-loss variant, a frameshift variant, an in-frame indel variant, or a variant that encodes a truncated FNIP1 variant polypeptide. In some embodiments, the FNIP1 variant nucleic acid molecule is a missense variant nucleic acid

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molecule. In some embodiments, the FNIP1 variant nucleic acid molecule comprises a single nucleotide polymorphism (SNP). In some embodiments, the FNIP1 variant nucleic acid molecule comprises a variation in a coding region. In some embodiments, the FNIP1 variant nucleic acid molecule does not comprise a variation in a non-coding region, except for a splice acceptor
5 region (two bases before the start of any exon except the first). In some embodiments, the FNIP1 variant nucleic acid molecule results or is predicted to result in a premature truncation of an FNIP1 polypeptide compared to the reference FNIP1. In some embodiments, the FNIP1 variant nucleic acid molecule is a variant that is predicted to be damaging to the protein function (and hence, in this case, protective to the human) by *in vitro* prediction algorithms
10 such as Polyphen, SIFT, or similar algorithms. In some embodiments, the FNIP1 variant nucleic acid molecule is a variant that causes or is predicted to cause a nonsynonymous amino acid substitution in an FNIP1 nucleic acid molecule and whose allele frequency is less than 1/100 alleles in the population from which the subject is selected. In some embodiments, the FNIP1 variant nucleic acid molecule is any rare missense variant (allele frequency < 0.1%; or 1 in 1,000
15 alleles), or any splice-site, stop-gain, start-loss, stop-loss, frameshift, or in-frame indel, or other frameshift FNIP1 variant.

In any of the embodiments described herein, the FLCN variant nucleic acid molecule can be any nucleic acid molecule (such as, a genomic nucleic acid molecule, an mRNA molecule, or a cDNA molecule produced from an mRNA molecule) encoding an FLCN variant polypeptide
20 having a partial loss-of-function, a complete loss-of-function, a predicted partial loss-of-function, or a predicted complete loss-of-function. A subject who has an FLCN polypeptide having a partial loss-of-function (or predicted partial loss-of-function) is hypomorphic for FLCN. In some embodiments, the FLCN variant nucleic acid molecule results in decreased or aberrant expression or activity of FLCN mRNA or polypeptide. In some embodiments, the FLCN variant
25 nucleic acid molecule is associated with a reduced *in vitro* response to FLCN ligands compared with reference FLCN. In some embodiments, the FLCN variant nucleic acid molecule is a splice-site variant, a stop-gain variant, a start-loss variant, a stop-loss variant, a frameshift variant, an in-frame indel variant, or a variant that encodes a truncated FLCN variant polypeptide. In some embodiments, the FLCN variant nucleic acid molecule is a missense variant nucleic acid
30 molecule. In some embodiments, the FLCN variant nucleic acid molecule comprises a single nucleotide polymorphism (SNP). In some embodiments, the FLCN variant nucleic acid molecule comprises a variation in a coding region. In some embodiments, the FLCN variant nucleic acid

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molecule does not comprise a variation in a non-coding region, except for a splice acceptor region (two bases before the start of any exon except the first). In some embodiments, the FLCN variant nucleic acid molecule results or is predicted to result in a premature truncation of an FLCN polypeptide compared to the reference FLCN. In some embodiments, the FLCN variant nucleic acid molecule is a variant that is predicted to be damaging to the protein function (and hence, in this case, protective to the human) by *in vitro* prediction algorithms such as Polyphen, SIFT, or similar algorithms. In some embodiments, the FLCN variant nucleic acid molecule is a variant that causes or is predicted to cause a nonsynonymous amino acid substitution in an FLCN nucleic acid molecule and whose allele frequency is less than 1/100 alleles in the population from which the subject is selected. In some embodiments, the FLCN variant nucleic acid molecule is any rare missense variant (allele frequency < 0.1%; or 1 in 1,000 alleles), or any splice-site, stop-gain, start-loss, stop-loss, frameshift, or in-frame indel, or other frameshift FLCN variant.

In any of the embodiments described herein, the FNIP1 variant genomic nucleic acid molecule may include one or more variations at any of the positions of chromosome 5 (i.e., positions 131,641,714-131,797,017) using the nucleotide sequence of the FNIP1 reference genomic nucleic acid molecule in the GRCh38/hg38 human genome assembly (see, ENSG00000217128.13, ENST00000510461.6 annotated in the in the Ensembl database (URL: world wide web at "http://useast.ensembl.org/Homo_sapiens/Gene/Summary?g=ENSG00000217128;r=5:131641714-131797017;transcript=ENST00000510461.6") as a reference sequence. The sequences provided in these transcripts for the FNIP1 genomic nucleic acid molecule are only exemplary sequences. Other sequences for the FNIP1 genomic nucleic acid molecule are also possible.

In any of the embodiments described herein, the FNIP1 variant nucleic acid molecule may comprise any one or more of the following genetic variations in the genomic nucleic acid molecule (referring to the chromosome:positions set forth in the GRCh38/hg38 human genome assembly): 5:131644687:A:G, 5:131644689:A:T, 5:131644701:G:A, 5:131644702:C:T, 5:131644707:T:C, 5:131644707:T:G, 5:131644708:A:C, 5:131644717:G:A, 5:131644717:G:T, 5:131644720:T:C, 5:131644721:G:C, 5:131644725:G:A, 5:131644726:C:T, 5:131644728:A:G, 5:131644734:G:A, 5:131644735:C:A, 5:131644735:C:T, 5:131644738:G:C, 5:131644744:G:A, 5:131644759:C:T, 5:131644761:A:G, 5:131647089:C:T, 5:131647090:C:A, 5:131647090:C:T, 5:131647091:C:A, 5:131647093:A:G, 5:131647093:A:T, 5:131647100:C:A, 5:131647106:G:C,

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 15 5:131796900:T:C, 5:131796901:C:G, 5:131796904:G:C, 5:131796906:A:G, 5:131796911:G:A,
 5:131796911:G:T, 5:131796912:T:A, 5:131796914:G:C, 5:131796915:G:A, or 5:131796917:G:A,
 or an mRNA molecule produced therefrom, or a cDNA molecule produced from the mRNA
 molecule.

For subjects that are genotyped or determined to be FNIP1 reference, such subjects
 20 have an increased risk of developing muscle disorder. For subjects that are genotyped or
 determined to be either FNIP1 reference or heterozygous for an FNIP1 variant nucleic acid
 molecule, such subjects can be treated with an FNIP1 inhibitor.

In any of the embodiments described herein, the FLCN variant genomic nucleic acid
 molecule may include one or more variations at any of the positions of chromosome 17 (i.e.,
 25 positions 17,212,212-17,237,188) using the nucleotide sequence of the FLCN reference
 genomic nucleic acid molecule in the GRCh38/hg38 human genome assembly (see,
 ENSG00000154803.13, ENST00000285071.9 annotated in the in the Ensembl database (URL:
 world wide web at "http://useast.ensembl.org/Homo_sapiens/Gene/Summary?
 g=ENSG00000154803;r=17:17212212-17237188;transcript=ENST00000285071.9")) as a
 30 reference sequence. The sequences provided in these transcripts for the FLCN genomic nucleic
 acid molecule are only exemplary sequences. Other sequences for the FLCN genomic nucleic
 acid molecule are also possible.

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In any of the embodiments described herein, the FLCN variant nucleic acid molecule may comprise any one or more of the following genetic variations in the genomic nucleic acid molecule (referring to the chromosome:positions set forth in the GRCh38/hg38 human genome assembly): 17:17213659:TTCCGAGAC:T, 17:17213680:G:T, 17:17213686:C:G, 17:17213686:C:T, 5 17:17213686:CG:C, 17:17213687:G:A, 17:17213695:G:A, 17:17213703:G:C, 17:17213705:G:A, 17:17213705:GT:G, 17:17213711:T:C, 17:17213712:G:C, 17:17213712:G:T, 17:17213737:C:T, 17:17213738:A:G, 17:17213747:G:C, 17:17213749:A:G, 17:17213758:T:C, 17:17213789:G:T, 17:17213796:C:G, 17:17213796:CTG:C, 17:17213798:G:A, 17:17213805:C:G, 17:17213815:C:CT, 17:17213815:C:T, 17:17213816:G:A, 17:17213823:C:CA, 17:17213834:A:C, 17:17213836:T:C, 10 17:17213848:T:C, 17:17213849:T:C, 17:17213852:C:T, 17:17213855:T:C, 17:17214984:C:G, 17:17214984:C:T, 17:17214993:C:G, 17:17214995:C:T, 17:17214996:C:A, 17:17215001:T:A, 17:17215001:T:G, 17:17215004:G:A, 17:17215006:C:T, 17:17215013:G:A, 17:17215015:C:T, 17:17215016:A:G, 17:17215022:C:A, 17:17215024:A:C, 17:17215036:G:A, 17:17215036:G:C, 17:17215037:A:C, 17:17215048:T:C, 17:17215057:G:C, 17:17215070:T:C, 17:17215073:T:G, 15 17:17215082:TG:T, 17:17215087:C:T, 17:17215184:C:G, 17:17215184:C:T, 17:17215188:G:A, 17:17215190:T:TC, 17:17215224:A:AC, 17:17215228:G:C, 17:17215236:TGA:T, 17:17215256:CA:C, 17:17215257:AC:A, 17:17215263:C:CAGGGTGG, 17:17215264:AGGGTGGAGGGTGGAACTGC:A, 17:17215282:T:TGCGGCTGCGTGGACCTC, 17:17215302:C:T, 17:17215311:CA:C, 17:17215313:A:C, 17:17215317:CTG:C, 17:17216382:G:A, 17:17216394:T:TG, 17:17216394:TG:T, 17:17216395:G:T, 20 17:17216400:G:A, 17:17216400:G:C, 17:17216400:G:T, 17:17216401:G:A, 17:17216401:G:T, 17:17216418:C:A, 17:17216418:C:CT, 17:17216424:C:A, 17:17216424:C:T, 17:17216426:C:CA, 17:17216427:AG:A, 17:17216433:T:C, 17:17216435:G:T, 17:17216440:G:A, 17:17216443:A:T, 17:17216453:G:C, 17:17216454:T:C, 17:17216458:G:A, 17:17216464:T:C, 17:17216466:T:C, 17:17216466:T:TA, 17:17216476:T:TG, 17:17216478:C:A, 17:17216479:G:C, 17:17216482:C:A, 25 17:17216484:C:A, 17:17216484:C:T, 17:17216485:A:G, 17:17216487:C:G, 17:17216491:C:CG, 17:17217068:C:G, 17:17217068:CCCGAAGTACTTCAAAAGCTGACT:C, 17:17217074:G:T, 17:17217086:C:G, 17:17217092:G:A, 17:17217112:C:CT, 17:17217116:TC:T, 17:17217124:A:T, 17:17217127:TG:T, 17:17217128:G:A, 17:17217133:C:T, 17:17217147:C:T, 17:17217161:G:A, 17:17217163:A:G, 17:17217168:AG:A, 17:17217174:AC:A, 17:17217175:C:A, 17:17217183:C:A, 17:17217184:T:A, 30 17:17217184:T:C, 17:17219017:A:C, 17:17219018:C:T, 17:17219030:G:A, 17:17219032:C:T, 17:17219033:G:A, 17:17219038:G:A, 17:17219038:G:T, 17:17219051:G:GCAGATCCGGGGCTGC, 17:17219082:TGAGA:T, 17:17219126:C:CTTCTGTACTCTCTGGCAACACAGGGGCT, 17:17219133:ACT:A, 17:17219147:CAG:C, 17:17219148:A:AG, 17:17219174:C:CA, 17:17219176:G:C, 17:17219177:A:G, 17:17219183:C:G, 17:17219187:GCTTT:G, 17:17219190:TTC:T, 17:17219194:G:C, 17:17219194:G:T,

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17:17228124:A:C, 17:17228133:T:C, 17:17228136:A:G, or 17:17228137:T:C,
or an mRNA molecule produced therefrom, or a cDNA molecule produced from the mRNA
5 molecule.

For subjects that are genotyped or determined to be FLCN reference, such subjects have an increased risk of developing muscle disorder. For subjects that are genotyped or determined to be either FLCN reference or heterozygous for an FLCN variant nucleic acid molecule, such subjects can be treated with an FLCN inhibitor.

10 In any of the embodiments described herein, the subject in whom muscle disorder is prevented by administering an FNIP1 inhibitor and/or an FLCN inhibitor may be anyone at risk for developing muscle disorder including, but not limited to, subjects with a genetic predisposition for developing muscle disorder. In some embodiments, administering an FNIP1 inhibitor and/or an FLCN inhibitor to a subject having muscle disorder may be carried out to
15 prevent development of another occurrence of muscle disorder in a subject who has already had muscle disorder. In any of the embodiments described herein, the methods can be used to improve muscle disorder.

In any of the embodiments described herein, the FNIP1 predicted loss-of-function polypeptide can be any FNIP1 polypeptide having a partial loss-of-function, a complete loss-of-
20 function, a predicted partial loss-of-function, or a predicted complete loss-of-function.

In any of the embodiments described herein, the FLCN predicted loss-of-function polypeptide can be any FLCN polypeptide having a partial loss-of-function, a complete loss-of-function, a predicted partial loss-of-function, or a predicted complete loss-of-function.

Any one or more (i.e., any combination) of the FNIP1 variant nucleic acid molecules
25 and/or FLCN variant nucleic acid molecules described herein can be used within any of the methods described herein to determine whether a subject has an increased or decreased risk of developing muscle disorder. The combinations of particular variants can form a mask used for statistical analysis of the particular correlation of FNIP1 and/or FLCN and an increased or decreased risk of developing muscle disorder. In some embodiments, the mask used for
30 statistical analysis of the particular correlation of FNIP1 and/or FLCN and an increased or decreased risk of developing muscle disorder can exclude any one or more of these FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecules described herein.

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In any of the embodiments described herein, the subject can have muscle disorder. In any of the embodiments described herein, the subject can be at risk of developing muscle disorder. In some embodiments, the muscle disorder comprises sarcopenia, Duchenne Muscular Dystrophy, and Pompe disease. In some embodiments, the muscle disorder
5 comprises sarcopenia. In some embodiments, the muscle disorder comprises Duchenne Muscular Dystrophy. In some embodiments, the muscle disorder comprises Pompe disease.

The present disclosure provides methods of treating a subject having muscle disorder or at risk of developing muscle disorder, the methods comprising administering an FNIP1 inhibitor and/or an FLCN inhibitor to the subject.

10 The present disclosure provides methods of treating a subject having a complication of muscle disorder or at risk of developing a complication of muscle disorder, the methods comprising administering an FNIP1 inhibitor and/or an FLCN inhibitor to the subject.

In some embodiments, the FNIP1 inhibitor comprises an inhibitory nucleic acid molecule. Examples of inhibitory nucleic acid molecules include, but are not limited to,
15 antisense nucleic acid molecules, small interfering RNAs (siRNAs), and short hairpin RNAs (shRNAs). Such inhibitory nucleic acid molecules can be designed to target any region of an FNIP1 nucleic acid molecule. In some embodiments, the antisense RNA, siRNA, or shRNA hybridizes to a sequence within an FNIP1 genomic nucleic acid molecule or mRNA molecule and decreases expression of the FNIP1 polypeptide in a cell in the subject. In some embodiments,
20 the FNIP1 inhibitor comprises an antisense molecule that hybridizes to an FNIP1 genomic nucleic acid molecule or mRNA molecule and decreases expression of the FNIP1 polypeptide in a cell in the subject. In some embodiments, the FNIP1 inhibitor comprises an siRNA that hybridizes to an FNIP1 genomic nucleic acid molecule or mRNA molecule and decreases expression of the FNIP1 polypeptide in a cell in the subject. In some embodiments, the FNIP1
25 inhibitor comprises an shRNA that hybridizes to an FNIP1 genomic nucleic acid molecule or mRNA molecule and decreases expression of the FNIP1 polypeptide in a cell in the subject.

In some embodiments, the FLCN inhibitor comprises an inhibitory nucleic acid molecule. Examples of inhibitory nucleic acid molecules include, but are not limited to, antisense nucleic acid molecules, small interfering RNAs (siRNAs), and short hairpin RNAs
30 (shRNAs). Such inhibitory nucleic acid molecules can be designed to target any region of an FLCN nucleic acid molecule. In some embodiments, the antisense RNA, siRNA, or shRNA hybridizes to a sequence within an FLCN genomic nucleic acid molecule or mRNA molecule and

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decreases expression of the FLCN polypeptide in a cell in the subject. In some embodiments, the FLCN inhibitor comprises an antisense molecule that hybridizes to an FLCN genomic nucleic acid molecule or mRNA molecule and decreases expression of the FLCN polypeptide in a cell in the subject. In some embodiments, the FLCN inhibitor comprises an siRNA that hybridizes to an
5 FLCN genomic nucleic acid molecule or mRNA molecule and decreases expression of the FLCN polypeptide in a cell in the subject. In some embodiments, the FLCN inhibitor comprises an shRNA that hybridizes to an FLCN genomic nucleic acid molecule or mRNA molecule and decreases expression of the FLCN polypeptide in a cell in the subject. Representative FLCN siRNA molecules are disclosed in, for example, WO 2022/178411.

10 The inhibitory nucleic acid molecules can comprise RNA, DNA, or both RNA and DNA. The inhibitory nucleic acid molecules can also be linked or fused to a heterologous nucleic acid sequence, such as in a vector, or a heterologous label. For example, the inhibitory nucleic acid molecules can be within a vector or as an exogenous donor sequence comprising the inhibitory nucleic acid molecule and a heterologous nucleic acid sequence. The inhibitory nucleic acid
15 molecules can also be linked or fused to a heterologous label. The label can be directly detectable (such as, for example, fluorophore) or indirectly detectable (such as, for example, hapten, enzyme, or fluorophore quencher). Such labels can be detectable by spectroscopic, photochemical, biochemical, immunochemical, or chemical means. Such labels include, for example, radiolabels, pigments, dyes, chromogens, spin labels, and fluorescent labels. The label
20 can also be, for example, a chemiluminescent substance; a metal-containing substance; or an enzyme, where there occurs an enzyme-dependent secondary generation of signal. The term "label" can also refer to a "tag" or hapten that can bind selectively to a conjugated molecule such that the conjugated molecule, when added subsequently along with a substrate, is used to generate a detectable signal. For example, biotin can be used as a tag along with an avidin or
25 streptavidin conjugate of horseradish peroxidase (HRP) to bind to the tag, and examined using a calorimetric substrate (such as, for example, tetramethylbenzidine (TMB)) or a fluorogenic substrate to detect the presence of HRP. Exemplary labels that can be used as tags to facilitate purification include, but are not limited to, myc, HA, FLAG or 3XFLAG, 6XHis or polyhistidine, glutathione-S-transferase (GST), maltose binding protein, an epitope tag, or the Fc portion of
30 immunoglobulin. Numerous labels include, for example, particles, fluorophores, haptens, enzymes and their calorimetric, fluorogenic and chemiluminescent substrates and other labels.

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The inhibitory nucleic acid molecules can comprise, for example, nucleotides or non-natural or modified nucleotides, such as nucleotide analogs or nucleotide substitutes. Such nucleotides include a nucleotide that contains a modified base, sugar, or phosphate group, or that incorporates a non-natural moiety in its structure. Examples of non-natural nucleotides
5 include, but are not limited to, dideoxynucleotides, biotinylated, aminated, deaminated, alkylated, benzylated, and fluorophor-labeled nucleotides.

The inhibitory nucleic acid molecules can also comprise one or more nucleotide analogs or substitutions. A nucleotide analog is a nucleotide which contains a modification to either the base, sugar, or phosphate moieties. Modifications to the base moiety include, but
10 are not limited to, natural and synthetic modifications of A, C, G, and T/U, as well as different purine or pyrimidine bases such as, for example, pseudouridine, uracil-5-yl, hypoxanthin-9-yl (I), and 2-aminoadenin-9-yl. Modified bases include, but are not limited to, 5-methylcytosine (5-me-C), 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine
15 and guanine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-halouracil and cytosine, 5-propynyl uracil and cytosine, 6-azo uracil, cytosine and thymine, 5-uracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl and other 8-substituted adenines and guanines, 5-halo (such as, for example, 5-bromo), 5-trifluoromethyl and other 5-substituted uracils and cytosines, 7-methylguanine, 7-methyladenine, 8-azaguanine, 8-azaadenine,
20 7-deazaguanine, 7-deazaadenine, 3-deazaguanine, and 3-deazaadenine.

Nucleotide analogs can also include modifications of the sugar moiety. Modifications to the sugar moiety include, but are not limited to, natural modifications of the ribose and deoxy ribose as well as synthetic modifications. Sugar modifications include, but are not limited to, the following modifications at the 2' position: OH; F; O-, S-, or N-alkyl; O-, S-, or N-alkenyl;
25 O-, S- or N-alkynyl; or O-alkyl-O-alkyl, wherein the alkyl, alkenyl, and alkynyl may be substituted or unsubstituted C₁₋₁₀alkyl or C₂₋₁₀alkenyl, and C₂₋₁₀alkynyl. Exemplary 2' sugar modifications also include, but are not limited to, -O[(CH₂)_nO]_mCH₃, -O(CH₂)_nOCH₃, -O(CH₂)_nNH₂, -O(CH₂)_nCH₃, -O(CH₂)_n-ONH₂, and -O(CH₂)_nON[(CH₂)_nCH₃]₂, where n and m, independently, are from 1 to about 10. Other modifications at the 2' position include, but are not limited to, C₁₋₁₀alkyl,
30 substituted lower alkyl, alkaryl, aralkyl, O-alkaryl or O-aralkyl, SH, SCH₃, OCN, Cl, Br, CN, CF₃, OCF₃, SOCH₃, SO₂CH₃, ONO₂, NO₂, N₃, NH₂, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino, substituted silyl, an RNA cleaving group, a reporter group, an

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intercalator, a group for improving the pharmacokinetic properties of an oligonucleotide, or a group for improving the pharmacodynamic properties of an oligonucleotide, and other substituents having similar properties. Similar modifications may also be made at other positions on the sugar, particularly the 3' position of the sugar on the 3' terminal nucleotide or in 2'-5' linked oligonucleotides and the 5' position of 5' terminal nucleotide. Modified sugars can also include those that contain modifications at the bridging ring oxygen, such as CH₂ and S. Nucleotide sugar analogs can also have sugar mimetics, such as cyclobutyl moieties in place of the pentofuranosyl sugar.

Nucleotide analogs can also be modified at the phosphate moiety. Modified phosphate moieties include, but are not limited to, those that can be modified so that the linkage between two nucleotides contains a phosphorothioate, chiral phosphorothioate, phosphorodithioate, phosphotriester, aminoalkylphosphotriester, methyl and other alkyl phosphonates including 3'-alkylene phosphonate and chiral phosphonates, phosphinates, phosphoramidates including 3'-amino phosphoramidate and aminoalkylphosphoramidates, thionophosphoramidates, thionoalkylphosphonates, thionoalkylphosphotriesters, and boranophosphates. These phosphate or modified phosphate linkage between two nucleotides can be through a 3'-5' linkage or a 2'-5' linkage, and the linkage can contain inverted polarity such as 3'-5' to 5'-3' or 2'-5' to 5'-2'. Various salts, mixed salts, and free acid forms are also included. Nucleotide substitutes also include peptide nucleic acids (PNAs).

In some embodiments, the antisense nucleic acid molecules are gapmers, whereby the first one to seven nucleotides at the 5' and 3' ends each have 2'-methoxyethyl (2'-MOE) modifications. In some embodiments, the first five nucleotides at the 5' and 3' ends each have 2'-MOE modifications. In some embodiments, the first one to seven nucleotides at the 5' and 3' ends are RNA nucleotides. In some embodiments, the first five nucleotides at the 5' and 3' ends are RNA nucleotides. In some embodiments, each of the backbone linkages between the nucleotides is a phosphorothioate linkage.

In some embodiments, the siRNA molecules have termini modifications. In some embodiments, the 5' end of the antisense strand is phosphorylated. In some embodiments, 5'-phosphate analogs that cannot be hydrolyzed, such as 5'-(E)-vinyl-phosphonate are used.

In some embodiments, the siRNA molecules have backbone modifications. In some embodiments, the modified phosphodiester groups that link consecutive ribose nucleosides have been shown to enhance the stability and *in vivo* bioavailability of siRNAs. The non-ester

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groups (-OH, =O) of the phosphodiester linkage can be replaced with sulfur, boron, or acetate to give phosphorothioate, boranophosphate, and phosphonoacetate linkages. In addition, substituting the phosphodiester group with a phosphotriester can facilitate cellular uptake of siRNAs and retention on serum components by eliminating their negative charge. In some

5 embodiments, the siRNA molecules have sugar modifications. In some embodiments, the sugars are deprotonated (reaction catalyzed by exo- and endonucleases) whereby the 2'-hydroxyl can act as a nucleophile and attack the adjacent phosphorous in the phosphodiester bond. Such alternatives include 2'-O-methyl, 2'-O-methoxyethyl, and 2'-fluoro modifications.

10 In some embodiments, the siRNA molecules have base modifications. In some embodiments, the bases can be substituted with modified bases such as pseudouridine, 5'-methylcytidine, N6-methyladenosine, inosine, and N7-methylguanosine.

In some embodiments, the siRNA molecules are conjugated to lipids. Lipids can be conjugated to the 5' or 3' termini of siRNA to improve their *in vivo* bioavailability by allowing

15 them to associate with serum lipoproteins. Representative lipids include, but are not limited to, cholesterol and vitamin E, and fatty acids, such as palmitate and tocopherol.

In some embodiments, a representative siRNA has the following formula:

Sense: mN*mN*/i2FN/mN/i2FN/mN/i2FN/mN/i2FN/mN/i2FN/mN/i2FN/mN/
i2FN/*mN*/32FN/

20 Antisense: /52FN/*i2FN/*mN/i2FN/mN/i2FN/mN/i2FN/mN/i2FN/mN/i2FN/mN/
i2FN/mN/i2FN/mN*N*N

wherein: "N" is the base; "2F" is a 2'-F modification; "m" is a 2'-O-methyl modification, "I" is an internal base; and "*" is a phosphorothioate backbone linkage.

In any of the embodiments described herein, the inhibitory nucleic acid molecules may

25 be administered, for example, as one to two hour i.v. infusions or s.c. injections. In any of the embodiments described herein, the inhibitory nucleic acid molecules may be administered at dose levels that range from about 50 mg to about 900 mg, from about 100 mg to about 800 mg, from about 150 mg to about 700 mg, or from about 175 mg to about 640 mg (2.5 to 9.14 mg/kg; 92.5 to 338 mg/m² – based on an assumption of a body weight of 70 kg and a

30 conversion of mg/kg to mg/m² dose levels based on a mg/kg dose multiplier value of 37 for humans).

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The present disclosure also provides vectors comprising any one or more of the inhibitory nucleic acid molecules. In some embodiments, the vectors comprise any one or more of the inhibitory nucleic acid molecules and a heterologous nucleic acid. The vectors can be viral or nonviral vectors capable of transporting a nucleic acid molecule. In some embodiments, the vector is a plasmid or cosmid (such as, for example, a circular double-stranded DNA into which additional DNA segments can be ligated). In some embodiments, the vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Expression vectors include, but are not limited to, plasmids, cosmids, retroviruses, adenoviruses, adeno-associated viruses (AAV), plant viruses such as cauliflower mosaic virus and tobacco mosaic virus, yeast artificial chromosomes (YACs), Epstein-Barr (EBV)-derived episomes, and other expression vectors known in the art.

The present disclosure also provides compositions comprising any one or more of the inhibitory nucleic acid molecules. In some embodiments, the composition is a pharmaceutical composition. In some embodiments, the compositions comprise a carrier and/or excipient. Examples of carriers include, but are not limited to, poly(lactic acid) (PLA) microspheres, poly(D,L-lactic-co-glycolic-acid) (PLGA) microspheres, liposomes, micelles, inverse micelles, lipid cochleates, and lipid microtubules. A carrier may comprise a buffered salt solution such as PBS, HBSS, etc.

In some embodiments, the FNIP1 inhibitor or FLCN inhibitor comprises a nuclease agent that induces one or more nicks or double-strand breaks at a recognition sequence(s) or a DNA-binding protein that binds to a recognition sequence within an FNIP1 or FLCN genomic nucleic acid molecule. The recognition sequence can be located within a coding region of the FNIP1 or FLCN gene, or within regulatory regions that influence the expression of the gene. A recognition sequence of the DNA-binding protein or nuclease agent can be located in an intron, an exon, a promoter, an enhancer, a regulatory region, or any non-protein coding region. The recognition sequence can include or be proximate to the start codon of the FNIP1 or FLCN gene. For example, the recognition sequence can be located about 10, about 20, about 30, about 40, about 50, about 100, about 200, about 300, about 400, about 500, or about 1,000 nucleotides from the start codon. As another example, two or more nuclease agents can be used, each targeting a nuclease recognition sequence including or proximate to the start codon. As another example, two nuclease agents can be used, one targeting a nuclease recognition sequence including or proximate to the start codon, and one targeting a nuclease recognition

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sequence including or proximate to the stop codon, wherein cleavage by the nuclease agents can result in deletion of the coding region between the two nuclease recognition sequences. Any nuclease agent that induces a nick or double-strand break into a desired recognition sequence can be used in the methods and compositions disclosed herein. Any DNA-binding
5 protein that binds to a desired recognition sequence can be used in the methods and compositions disclosed herein.

Suitable nuclease agents and DNA-binding proteins for use herein include, but are not limited to, zinc finger protein or zinc finger nuclease (ZFN) pair, Transcription Activator-Like Effector (TALE) protein or Transcription Activator-Like Effector Nuclease (TALEN), or Clustered
10 Regularly Interspersed Short Palindromic Repeats (CRISPR)/CRISPR-associated (Cas) systems. The length of the recognition sequence can vary, and includes, for example, recognition sequences that are about 30-36 bp for a zinc finger protein or ZFN pair, about 15-18 bp for each ZFN, about 36 bp for a TALE protein or TALEN, and about 20 bp for a CRISPR/Cas guide RNA.

In some embodiments, CRISPR/Cas systems can be used to modify FNIP1 or FLCN
15 genomic nucleic acid molecule within a cell. The methods and compositions disclosed herein can employ CRISPR-Cas systems by utilizing CRISPR complexes (comprising a guide RNA (gRNA) complexed with a Cas protein) for site-directed cleavage of FNIP1 or FLCN nucleic acid molecules.

Cas proteins generally comprise at least one RNA recognition or binding domain that
20 can interact with gRNAs. Cas proteins can also comprise nuclease domains (such as, for example, DNase or RNase domains), DNA binding domains, helicase domains, protein-protein interaction domains, dimerization domains, and other domains. Suitable Cas proteins include, for example, a wild type Cas9 protein and a wild type Cpf1 protein (such as, for example, FnCpf1). A Cas protein can have full cleavage activity to create a double-strand break in an
25 FNIP1 or FLCN genomic nucleic acid molecule or it can be a nickase that creates a single-strand break in an FNIP1 or FLCN genomic nucleic acid molecule. Additional examples of Cas proteins include, but are not limited to, Cas1, Cas1B, Cas2, Cas3, Cas4, Cas5, Cas5e (CasD), Cas6, Cas6e, Cas6f, Cas7, Cas8a1, Cas8a2, Cas8b, Cas8c, Cas9 (Csn1 or Csx12), Cas10, Cas10d, CasF, CasG, CasH, Csy1, Csy2, Csy3, Cse1 (CasA), Cse2 (CasB), Cse3 (CasE), Cse4 (CasC), Csc1, Csc2, Csa5,
30 Csn2, Csm2, Csm3, Csm4, Csm5, Csm6, Cmr1, Cmr3, Cmr4, Cmr5, Cmr6, Csb1, Csb2, Csb3, Csx17, Csx14, Csx10, Csx16, CsaX, Csx3, Csx1, Csx15, Csf1, Csf2, Csf3, Csf4, and Cu1966, and homologs or modified versions thereof. In some embodiments, a Cas system, such as Cas12a,

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can have multiple gRNAs encoded into a single crRNA. Cas proteins can also be operably linked to heterologous polypeptides as fusion proteins. For example, a Cas protein can be fused to a cleavage domain, an epigenetic modification domain, a transcriptional activation domain, or a transcriptional repressor domain. Cas proteins can be provided in any form. For example, a Cas protein can be provided in the form of a protein, such as a Cas protein complexed with a gRNA. Alternately, a Cas protein can be provided in the form of a nucleic acid molecule encoding the Cas protein, such as an RNA or DNA.

In some embodiments, targeted genetic modifications of FNIP1 or FLCN genomic nucleic acid molecules can be generated by contacting a cell with a Cas protein and one or more gRNAs that hybridize to one or more gRNA recognition sequences within a target genomic locus in the FNIP1 or FLCN genomic nucleic acid molecule. The gRNA recognition sequence can include or be proximate to the start codon of an FNIP1 or FLCN genomic nucleic acid molecule or the stop codon of an FNIP1 or FLCN genomic nucleic acid molecule. For example, the gRNA recognition sequence can be located from about 10, from about 20, from about 30, from about 40, from about 50, from about 100, from about 200, from about 300, from about 400, from about 500, or from about 1,000 nucleotides of the start codon or the stop codon.

The gRNA recognition sequences within a target genomic locus in an FNIP1 or FLCN genomic nucleic acid molecule are located near a Protospacer Adjacent Motif (PAM) sequence, which is a 2-6 base pair DNA sequence immediately following the DNA sequence targeted by the Cas9 nuclease. The canonical PAM is the sequence 5'-NGG-3' where "N" is any nucleobase followed by two guanine ("G") nucleobases. gRNAs can transport Cas9 to anywhere in the genome for gene editing, but no editing can occur at any site other than one at which Cas9 recognizes PAM. In addition, 5'-NGA-3' can be a highly efficient non-canonical PAM for human cells. Generally, the PAM is about 2-6 nucleotides downstream of the DNA sequence targeted by the gRNA. The PAM can flank the gRNA recognition sequence. In some embodiments, the gRNA recognition sequence can be flanked on the 3' end by the PAM. In some embodiments, the gRNA recognition sequence can be flanked on the 5' end by the PAM. For example, the cleavage site of Cas proteins can be about 1 to about 10, about 2 to about 5 base pairs, or three base pairs upstream or downstream of the PAM sequence. In some embodiments (such as when Cas9 from *S. pyogenes* or a closely related Cas9 is used), the PAM sequence of the non-complementary strand can be 5'-NGG-3', where N is any DNA nucleotide and is immediately 3' of the gRNA recognition sequence of the non-complementary strand of the target DNA. As

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such, the PAM sequence of the complementary strand would be 5'-CCN-3', where N is any DNA nucleotide and is immediately 5' of the gRNA recognition sequence of the complementary strand of the target DNA.

A gRNA is an RNA molecule that binds to a Cas protein and targets the Cas protein to a specific location within an FNIP1 or FLCN genomic nucleic acid molecule. An exemplary gRNA is a gRNA effective to direct a Cas enzyme to bind to or cleave an FNIP1 or FLCN genomic nucleic acid molecule, wherein the gRNA comprises a DNA-targeting segment that hybridizes to a gRNA recognition sequence within the FNIP1 or FLCN genomic nucleic acid molecule. Exemplary gRNAs comprise a DNA-targeting segment that hybridizes to a gRNA recognition sequence present within an FNIP1 or FLCN genomic nucleic acid molecule that includes or is proximate to the start codon or the stop codon. For example, a gRNA can be selected such that it hybridizes to a gRNA recognition sequence that is located from about 5, from about 10, from about 15, from about 20, from about 25, from about 30, from about 35, from about 40, from about 45, from about 50, from about 100, from about 200, from about 300, from about 400, from about 500, or from about 1,000 nucleotides of the start codon or located from about 5, from about 10, from about 15, from about 20, from about 25, from about 30, from about 35, from about 40, from about 45, from about 50, from about 100, from about 200, from about 300, from about 400, from about 500, or from about 1,000 nucleotides of the stop codon. Suitable gRNAs can comprise from about 17 to about 25 nucleotides, from about 17 to about 23 nucleotides, from about 18 to about 22 nucleotides, or from about 19 to about 21 nucleotides. In some embodiments, the gRNAs can comprise 20 nucleotides.

The Cas protein and the gRNA form a complex, and the Cas protein cleaves the FNIP1 or FLCN genomic nucleic acid molecule. The Cas protein can cleave the nucleic acid molecule at a site within or outside of the nucleic acid sequence present in the FNIP1 or FLCN genomic nucleic acid molecule to which the DNA-targeting segment of a gRNA will bind. For example, formation of a CRISPR complex (comprising a gRNA hybridized to a gRNA recognition sequence and complexed with a Cas protein) can result in cleavage of one or both strands in or near (such as, for example, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 50, or more base pairs from) the nucleic acid sequence present in the FNIP1 or FLCN genomic nucleic acid molecule to which a DNA-targeting segment of a gRNA will bind.

Such methods can result, for example, in an FNIP1 or FLCN genomic nucleic acid molecule in which a region of the FNIP1 or FLCN genomic nucleic acid molecule is disrupted, the

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start codon is disrupted, the stop codon is disrupted, or the coding sequence is disrupted or deleted. Optionally, the cell can be further contacted with one or more additional gRNAs that hybridize to additional gRNA recognition sequences within the target genomic locus in the FNIP1 or FLCN genomic nucleic acid molecule. By contacting the cell with one or more
5 additional gRNAs (such as, for example, a second gRNA that hybridizes to a second gRNA recognition sequence), cleavage by the Cas protein can create two or more double-strand breaks or two or more single-strand breaks.

In some embodiments, the FNIP1 and/or FLCN gRNA molecules can be pooled. For example, the FNIP1 gRNA molecules can be pooled in 15 gRNAs per gene, and can be packaged
10 as multiple (4, 5, or 6, for example) gRNAs per vector (for example, AAV). Likewise, the FLCN gRNA molecules can be pooled in 15 gRNAs per gene, and can be packaged as multiple (4, 5, or 6, for example) gRNAs per vector (for example, AAV).

In any of the methods of treatment or prevention described herein, the subject being treated may comprise an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic
15 acid molecule. In some embodiments, the subject being treated is heterozygous for the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule. In some embodiments, the subject being treated is homozygous for the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule. In some embodiments, the subject being treated is FNIP1 and/or FLCN reference. The FNIP1 variant nucleic acid molecule and/or
20 an FLCN variant nucleic acid molecule can be any of the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecules disclosed herein. In some embodiments, the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule is a FNIP1 or FLCN variant genomic nucleic acid molecule that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA
25 molecule produced from the mRNA molecule.

In some embodiments, the methods of treatment or prevention further comprise detecting the presence or absence of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule in a biological sample from the subject. In some embodiments, the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule can be
30 any of the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecules disclosed herein. In some embodiments, the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule is an FNIP1 or FLCN variant genomic nucleic acid molecule

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that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule.

The present disclosure also provides methods of treating a subject with a muscle disorder therapeutic agent, wherein the subject has muscle disorder or is at risk of developing muscle disorder. The methods comprise determining whether the subject has an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule by obtaining or having obtained a biological sample from the subject, and performing or having performed a sequence analysis on the biological sample to determine if the subject has a genotype comprising the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule. In embodiments where the subject is FNIP1 and/or FLCN reference, the methods further comprise administering or continuing to administer the muscle disorder therapeutic agent in a standard dosage amount to the subject, and/or administering an FNIP1 inhibitor and/or an FLCN inhibitor to the subject. In embodiments where the subject is heterozygous for the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, the methods further comprise administering or continuing to administer the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount to the subject, and/or administering an FNIP1 inhibitor and/or an FLCN inhibitor to the subject. In embodiments where the subject is homozygous for the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, the methods further comprise administering or continuing to administer the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount. The presence of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule indicates the subject has a decreased risk of developing muscle disorder. In some embodiments, the subject is FNIP1 and/or FLCN reference. In some embodiments, the subject is heterozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule. In some embodiments, the subject is homozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule. In any of the embodiments described herein, the FNIP1 inhibitor or FLCN inhibitor is an example of a muscle disorder therapeutic agent. In some embodiments, the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule is a FNIP1 or FLCN variant genomic nucleic acid molecule that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule.

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For subjects that are genotyped or determined to be either FNIP1 and/or FLCN reference or heterozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, such subjects can be administered an FNIP1 inhibitor and/or an FLCN inhibitor, as described herein.

5 Detecting the presence or absence of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule in a biological sample from a subject and/or determining whether a subject has an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule can be carried out by any of the methods described herein. In some embodiments, these methods can be carried out *in vitro*. In some embodiments, these
10 methods can be carried out *in situ*. In some embodiments, these methods can be carried out *in vivo*. In any of these embodiments, the nucleic acid molecule can be present within a cell obtained from the subject.

 In some embodiments, when the subject is FNIP1 reference, the subject is administered a muscle disorder therapeutic agent in an amount that is the same as or less than
15 a standard dosage amount, and/or an FNIP1 inhibitor. In some embodiments, when the subject is heterozygous for an FNIP1 variant nucleic acid molecule, the subject is administered a muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and/or an FNIP1 inhibitor.

 In some embodiments, when the subject is FLCN reference, the subject is administered
20 a muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and/or an FLCN inhibitor. In some embodiments, when the subject is heterozygous for an FLCN variant nucleic acid molecule, the subject is administered a muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and/or an FLCN inhibitor.

25 In some embodiments, the treatment or prevention methods comprise detecting the presence or absence of a decrease in the expression of an FNIP1 variant mRNA or polypeptide and/or FLCN variant mRNA or polypeptide in a biological sample from the subject. In some embodiments, when the subject does not have a decrease in the expression of an FNIP1 variant mRNA or polypeptide and/or FLCN variant mRNA or polypeptide, the subject is administered a
30 muscle disorder therapeutic agent in a standard dosage amount, and/or an FNIP1 inhibitor and/or an FLCN inhibitor. In some embodiments, when the subject has a decrease in the expression of an FNIP1 variant mRNA or polypeptide and/or FLCN variant mRNA or polypeptide,

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the subject is administered a muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount.

The present disclosure also provides methods of treating a subject with a muscle disorder therapeutic agent, wherein the subject has muscle disorder or is at risk of developing muscle disorder. The methods comprise determining whether the subject has a decrease in the expression of an FNIP1 variant mRNA or polypeptide and/or an FLCN variant mRNA or polypeptide by obtaining or having obtained a biological sample from the subject, and performing or having performed an assay on the biological sample to determine if the subject a decrease in the expression of an FNIP1 variant mRNA or polypeptide and/or an FLCN variant mRNA or polypeptide. In embodiments where the subject does not have a decrease in the expression of an FNIP1 variant mRNA or polypeptide and/or an FLCN variant mRNA or polypeptide, the methods further comprise administering or continuing to administer the muscle disorder therapeutic agent in a standard dosage amount to the subject, and/or administering an FNIP1 inhibitor and/or an FLCN inhibitor to the subject. In embodiments where the subject has a decrease in the expression of an FNIP1 variant mRNA or polypeptide and/or an FLCN variant mRNA or polypeptide, the methods further comprise administering or continuing to administer the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount to the subject. The presence of a decrease in the expression of an FNIP1 variant mRNA or polypeptide and/or an FLCN variant mRNA or polypeptide indicates the subject has a decreased risk of developing muscle disorder. In some embodiments, the subject has a decrease in the expression of an FNIP1 variant mRNA or polypeptide and/or an FLCN variant mRNA or polypeptide. In some embodiments, the subject does not have a decrease in the expression of an FNIP1 variant mRNA or polypeptide and/or an FLCN variant mRNA or polypeptide. In any of the embodiments described herein, the FNIP1 inhibitor or FLCN inhibitor is an example of a muscle disorder therapeutic agent. In some embodiments, the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule is an FNIP1 variant genomic nucleic acid molecule or FLCN variant genomic nucleic acid molecule that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule.

Detecting a decrease in the expression of an FNIP1 variant mRNA or polypeptide and/or an FLCN variant mRNA or polypeptide can be carried out by a variety of known

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methods. In some embodiments, these methods can be carried out *in vitro*. In some embodiments, these methods can be carried out *in situ*. In some embodiments, these methods can be carried out *in vivo*. In any of these embodiments, the mRNA or polypeptide can be present within a cell obtained from the subject.

5 In some embodiments, the treatment or prevention methods comprise detecting the presence or absence of an FNIP1 variant polypeptide and/or an FLCN variant polypeptide in a biological sample from the subject. In some embodiments, when the subject does not have an FNIP1 variant polypeptide and/or an FLCN variant polypeptide, the subject is administered a muscle disorder therapeutic agent in an amount that is the same as or less than a standard
10 dosage amount, and/or an FNIP1 inhibitor and/or an FLCN inhibitor. In some embodiments, when the subject has an FNIP1 variant polypeptide and/or an FLCN variant polypeptide, the subject is administered a muscle disorder therapeutic agent in standard dosage amount.

 The present disclosure also provides methods of treating a subject with a muscle disorder therapeutic agent, wherein the subject has muscle disorder or is at risk of developing
15 muscle disorder. The methods comprise determining whether the subject has an FNIP1 variant polypeptide and/or an FLCN variant polypeptide by obtaining or having obtained a biological sample from the subject and performing or having performed an assay on the biological sample to determine if the subject has an FNIP1 variant polypeptide and/or an FLCN variant
20 polypeptide. When the subject does not have an FNIP1 variant polypeptide and/or an FLCN variant polypeptide, the subject is administered the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and/or an FNIP1 inhibitor and/or an FLCN inhibitor. When the subject has an FNIP1 variant polypeptide and/or an FLCN variant polypeptide, the subject is administered the muscle disorder therapeutic agent in a standard dosage amount. The presence of an FNIP1 variant polypeptide and/or an FLCN variant
25 polypeptide indicates the subject has a decreased risk of developing muscle disorder. In some embodiments, the subject has an FNIP1 variant polypeptide and/or an FLCN variant polypeptide. In some embodiments, the subject does not have an FNIP1 variant polypeptide and/or an FLCN variant polypeptide.

 The present disclosure also provides methods of preventing a subject from developing
30 muscle disorder by administering a muscle disorder therapeutic agent. In some embodiments, the method comprises determining whether the subject has an FNIP1 variant polypeptide and/or an FLCN variant polypeptide by obtaining or having obtained a biological sample from

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the subject and performing or having performed an assay on the biological sample to determine if the subject has an FNIP1 variant polypeptide and/or an FLCN variant polypeptide. When the subject does not have an FNIP1 variant polypeptide and/or an FLCN variant polypeptide, the subject is administered the muscle disorder therapeutic agent in an amount
5 that is the same as or less than a standard dosage amount, and/or an FNIP1 inhibitor and/or an FLCN inhibitor. When the subject has an FNIP1 variant polypeptide and/or an FLCN variant polypeptide, the subject is administered the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount. The presence of an FNIP1 variant polypeptide and/or an FLCN variant polypeptide indicates the subject has a decreased risk of
10 developing muscle disorder. In some embodiments, the subject has an FNIP1 variant polypeptide and/or an FLCN variant polypeptide. In some embodiments, the subject does not have an FNIP1 variant polypeptide and/or an FLCN variant polypeptide.

Detecting the presence or absence of an FNIP1 variant polypeptide and/or an FLCN variant polypeptide in a biological sample from a subject and/or determining whether a subject
15 has an FNIP1 variant polypeptide and/or an FLCN variant polypeptide can be carried out by any of the methods described herein. In some embodiments, these methods can be carried out *in vitro*. In some embodiments, these methods can be carried out *in situ*. In some embodiments, these methods can be carried out *in vivo*. In any of these embodiments, the polypeptide can be present within a cell obtained from the subject.

20 In some embodiments, the FNIP1 inhibitor and/or FLCN inhibitor is a small molecule. In some embodiments, the small molecule is low molecular weight (< 900 daltons) organic compound.

In some embodiments, the FNIP1 inhibitor and/or FLCN inhibitor comprises an antibody, or antigen-binding fragment thereof. In some embodiments, the antibody, or
25 antigen-binding fragment thereof, binds specifically to human FNIP1 or FLCN. In some embodiments, the antibody is a fully human monoclonal antibody (mAb), or antigen-binding fragment thereof, that specifically binds and neutralizes, inhibits, blocks, abrogates, reduces, or interferes with, at least one activity of FNIP1 or FLCN, in particular, human FNIP1 or FLCN. In some embodiments, an antibody or fragment thereof can neutralize, inhibit, block, abrogate,
30 reduce, or interfere with, an activity of FNIP1 or FLCN by binding to an epitope of FNIP1 or FLCN that is directly involved in the targeted activity of FNIP1 or FLCN. In some embodiments, an antibody or fragment thereof can neutralize, inhibit, block, abrogate, reduce, or interfere with,

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an activity of FNIP1 or FLCN by binding to an epitope of FNIP1 or FLCN that is not directly involved in the targeted activity of FNIP1 or FLCN, but the antibody or fragment binding thereto sterically or conformationally inhibits, blocks, abrogates, reduces, or interferes with, the targeted activity of FNIP1 or FLCN. In some embodiments, an antibody or fragment thereof
5 binds to an epitope of FNIP1 or FLCN that is not directly involved in the targeted activity of FNIP1 or FLCN (i.e., a non-blocking antibody), but the antibody or fragment binding thereto results in the enhancement of the clearance of FNIP1 or FLCN from the circulation, compared to the clearance of FNIP1 or FLCN in the absence of the antibody or fragment thereof, thereby indirectly inhibiting, blocking, abrogating, reducing, or interfering with, an activity of FNIP1 or
10 FLCN. Clearance of FNIP1 or FLCN from the circulation can be particularly enhanced by combining two or more different non-blocking antibodies that do not compete with one another for specific binding to FNIP1 or FLCN. The antibodies can be full-length (for example, an IgG1 or IgG4 antibody) or may comprise only an antigen-binding portion (for example, a Fab, F(ab')₂ or scFv fragment), and may be modified to affect functionality, e.g., to eliminate residual
15 effector functions (Reddy et al., J. Immunol., 2000, 164, 1925-1933).

In some embodiments, the antibody or antigen-binding fragment thereof specifically binds to FNIP1 or FLCN with an equilibrium dissociation constant (K_D) of about 7 nM or less, about 6 nM or less, about 5 nM or less, about 4 nM or less, about 3 nM or less, about 2 nM or less, or about 1 nM or less, as measured by surface plasmon resonance assay (for example,
20 BIACORE™). In some embodiments, the antibody exhibits a K_D of about 800 pM or less, about 700 pM or less; about 600 pM or less; about 500 pM or less; about 400 pM or less; about 300 pM or less; about 200 pM or less; about 100 pM or less; or about 50 pM or less.

In some embodiments, the anti-FNIP1 antibodies and/or anti-FLCN antibodies have a modified glycosylation pattern. In some applications, modification to remove undesirable
25 glycosylation sites may be useful, or e.g., removal of a fucose moiety to increase antibody dependent cellular cytotoxicity (ADCC) function (see, Shield et al., J. Biol. Chem., 2002, 277, 26733). In other applications, removal of N-glycosylation site may reduce undesirable immune reactions against the therapeutic antibodies or increase affinities of the antibodies. In yet other applications, modification of galactosylation can be made in order to modify complement
30 dependent cytotoxicity (CDC).

In some embodiments, the muscle disorder therapeutic agent includes, but is not limited to, a glucocorticosteroid (such as, for example, prednisone, prednisolone, deflazacort,

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and others), testosterone and other androgenic hormones or analogues, or an androgen receptor modulator (such as, for example, enobosarm), ataluren, an oligonucleotide (such as, for example, eteplirsen, golodirsen, viltolarsen, and casimersen), losmapimod, zetomipzomib, venoglobulin-IH, an activin II receptor antagonist (such as, for example, bimagrumab), a
5 myostatin inhibitor (such as, for example, trevogrumab and domagrozumab), an activin A antagonist (such as, for example, garetosmab), and reldesemtiv.

The present disclosure also provides compositions comprising a combination of an antibody or antigen-binding fragment thereof and a muscle disorder therapeutic agent.

In some embodiments, the muscle disorder therapeutic agent can be combined with
10 an FNIP1 inhibitor and/or an FLCN inhibitor.

In some embodiments, the dose of the muscle disorder therapeutic agents can be decreased by about 10%, by about 20%, by about 30%, by about 40%, by about 50%, by about 60%, by about 70%, by about 80%, or by about 90% for subjects that are heterozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule or FNIP1
15 reference and/or FLCN reference (i.e., a less than the standard dosage amount) compared to subjects that are homozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule (who may receive a standard dosage amount). In some embodiments, the dose of the muscle disorder therapeutic agents can be decreased by about 10%, by about 20%, by about 30%, by about 40%, or by about 50%. In some embodiments, the
20 dose of the muscle disorder therapeutic agents can be decreased by about 10%, by about 20%, by about 30%, by about 40%, by about 50%, by about 60%, by about 70%, by about 80%, or by about 90% for subjects that are heterozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule compared to subjects that are or FNIP1 reference and/or FLCN reference. In addition, subjects that are heterozygous for an FNIP1 variant nucleic acid
25 molecule and/or an FLCN variant nucleic acid molecule or or FNIP1 reference and/or FLCN reference can be administered the muscle disorder therapeutic agents less frequently compared to subjects that are heterozygous for the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule.

Administration of the muscle disorder therapeutic agents and/or FNIP1 inhibitors
30 and/or FLCN inhibitors can be repeated, for example, after one day, two days, three days, five days, one week, two weeks, three weeks, one month, five weeks, six weeks, seven weeks, eight weeks, two months, or three months. The repeated administration can be at the same dose or

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at a different dose. The administration can be repeated once, twice, three times, four times, five times, six times, seven times, eight times, nine times, ten times, or more. For example, according to certain dosage regimens a subject can receive therapy for a prolonged period of time such as, for example, 6 months, 1 year, or more.

5 Administration of the muscle disorder therapeutic agents and/or FNIP1 inhibitors and/or FLCN inhibitors can occur by any suitable route including, but not limited to, parenteral, intravenous, oral, subcutaneous, intra-arterial, intracranial, intrathecal, intraperitoneal, topical, intranasal, or intramuscular. Pharmaceutical compositions for administration are desirably sterile and substantially isotonic and manufactured under GMP conditions. Pharmaceutical
10 compositions can be provided in unit dosage form (i.e., the dosage for a single administration). Pharmaceutical compositions can be formulated using one or more physiologically and pharmaceutically acceptable carriers, diluents, excipients, or auxiliaries. The formulation depends on the route of administration chosen. The term "pharmaceutically acceptable" means that the carrier, diluent, excipient, or auxiliary is compatible with the other ingredients of the
15 formulation and not substantially deleterious to the recipient thereof.

The terms "treat", "treating", and "treatment" and "prevent", "preventing", and "prevention" as used herein, refer to eliciting the desired biological response, such as a therapeutic and prophylactic effect, respectively. In some embodiments, a therapeutic effect comprises one or more of a decrease/reduction in muscle disorder, a decrease/reduction in the
20 severity of muscle disorder (such as, for example, a reduction or inhibition of development of muscle disorder), a decrease/reduction in symptoms and disease-related effects, delaying the onset of symptoms and disease-related effects, reducing the severity of symptoms of disease-related effects, reducing the number of symptoms and disease-related effects, reducing the latency of symptoms and disease-related effects, an amelioration of symptoms and disease-
25 related effects, reducing secondary symptoms, reducing secondary infections, preventing relapse to muscle disorder, decreasing the number or frequency of relapse episodes, increasing latency between symptomatic episodes, increasing time to sustained progression, speeding recovery, or increasing efficacy of or decreasing resistance to alternative therapeutics, and/or an increased survival time of the affected host animal, following administration of the agent or
30 composition comprising the agent. A prophylactic effect may comprise a complete or partial avoidance/inhibition or a delay of muscle disorder development/progression (such as, for example, a complete or partial avoidance/inhibition or a delay), and an increased survival time

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of the affected host animal, following administration of a therapeutic protocol. Treatment of muscle disorder encompasses the treatment of a subject already diagnosed as having any form of muscle disorder at any clinical stage or manifestation, the delay of the onset or evolution or aggravation or deterioration of the symptoms or signs of muscle disorder, and/or preventing
5 and/or reducing the severity of muscle disorder.

In some embodiments, the FNIP1 inhibitor and/or FLCN inhibitor and the muscle disorder therapeutic agent are disposed within a pharmaceutical composition. In some embodiments, the FNIP1 inhibitor and/or FLCN inhibitor is disposed within a first pharmaceutical composition and the muscle disorder therapeutic agent is disposed within a
10 second pharmaceutical composition. In some embodiments, the first pharmaceutical composition and the second pharmaceutical composition are administered simultaneously. In some embodiments, the first pharmaceutical composition is administered before the second pharmaceutical composition. In some embodiments, the first pharmaceutical composition is administered after the second pharmaceutical composition.

15 In any of the embodiments described herein, administration of the FNIP1 inhibitor and/or FLCN inhibitor can be targeted to a specific tissue. For example, in some embodiments, the FNIP1 inhibitor and/or FLCN inhibitor can be targeted to muscle tissue, muscle cells, skeletal muscle tissue, or skeletal muscle cells. In some embodiments described herein, administration of the FNIP1 inhibitor and/or FLCN inhibitor can be targeted to muscle tissue,
20 muscle cells, skeletal muscle tissue, or skeletal muscle cells. For example, the FNIP1 inhibitor and/or FLCN inhibitor can be linked to CACNG1 antibody, or an antigen-binding fragment thereof. In some embodiments, a muscle-specific FNIP1 siRNA (CACNG1 mAB-siRNA) is used to promote oxidative metabolism and lysosomal biogenesis in muscle fibers.

In some embodiments, the CACNG1 antibody, or antigen-binding fragment thereof,
25 comprises a heavy chain CDR1 (HCDR1) comprising an amino acid sequence selected from any of the HCDR1 amino acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In some embodiments, the CACNG1 antibody, or antigen-binding fragment thereof, comprises a heavy chain CDR2 (HCDR2) comprising an amino acid sequence selected from any of the HCDR2 amino
30 acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In some embodiments, the CACNG1 antibody, or antigen-binding fragment thereof, comprises a heavy chain CDR3 (HCDR3)

comprising an amino acid sequence selected from any of the HCDR3 amino acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In some embodiments, the CACNG1 antibody, or antigen-binding fragment thereof, comprises a light chain CDR1 (LCDR1) comprising an amino acid sequence selected from any of the LCDR1 amino acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In some embodiments, the CACNG1 antibody, or antigen-binding fragment thereof, comprises a light chain CDR2 (LCDR2) comprising an amino acid sequence selected from any of the LCDR2 amino acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. In some embodiments, the CACNG1 antibody, or antigen-binding fragment thereof, comprises a light chain CDR3 (LCDR3) comprising an amino acid sequence selected from any of the LCDR3 amino acid sequences listed in Table 1 or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

In some embodiments, the CACNG1 antibody, or antigen-binding fragment thereof, comprises an HCVR amino acid sequence listed in Table 1, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto. In some embodiments, the CACNG1 antibody, or antigen-binding fragment thereof, comprises an LCVR amino acid sequence listed in Table 1, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

In some embodiments, the CACNG1 antibody, or antigen-binding fragment thereof, comprises an HC amino acid sequence selected from any one of SEQ ID NO: 97 to SEQ ID NO: 108, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto. In some embodiments, the CACNG1 antibody, or antigen-binding fragment thereof, comprises an LC amino acid sequence selected from any one of SEQ ID NO: 109 to SEQ ID NO: 120, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity thereto.

Table 1: anti-CACNG1 Antibodies

Antibody Designation	SEQ ID NOs:							
	Heavy Chain				Light Chain			
	VR	CDR1	CDR2	CDR3	VR	CDR1	CDR2	CDR3
1	1	13	25	37	49	61	73	85
2	2	14	26	38	50	62	74	86
3	3	15	27	39	51	63	75	87
4	4	16	28	40	52	64	76	88
5	5	17	29	41	53	65	77	89
6	6	18	30	42	54	66	78	90
7	7	19	31	43	55	67	79	91
8	8	20	32	44	56	68	80	92
9	9	21	33	45	57	69	81	93
10	10	22	34	46	58	70	82	94
11	11	23	35	47	59	71	83	95
12	12	24	36	48	60	72	84	96

HCVR Amino Acid Sequences:

- QVQLVESGGGVVQPGRLRLSCTASGITFRNYGMHWVRQAPGKGLEWVAVMWYDGSNKYYADSVKGRF
TISGDNSKVYLQMNSLRAEDTAVYYCARRGTIRTAAPFDYWGGTLTVSS (SEQ ID NO: 1);
- 5 QVQLQQWGAGLLKPSATLSRTCAYVGGSFSGYYWNWIRQSPGKLEWIGEILHSGRTNYPNPSLKSRTISV
DTSKNQFSLKLTSVTAADTAVYYCAGRIAARHGWFDPWGGTLTVSS (SEQ ID NO: 2);
QVQLVESGGGVVQPGRLRLSCAASGFTFSTYGMHWVRQAPGKLEWVAVIWHDGSDKYYVDSVKGRFS
IARDNSKNTLYLQMNSLRVEDTGIYYCARRGIRGTVFDHWGLGTLTVSS (SEQ ID NO: 3);
QVQLQESGPGLVKPSSETLSLTCTVSGDSINNYWTWLRQPPGKLEWIGIYYSGSANYPNPSLKSRTISVDT
- 10 SKNQFSLKLNSTAAADTAVYYCARGAVKYFRHWGGTLTVSS (SEQ ID NO: 4);
QVQLVESGGGVVQPGTSLRLSCAASGFTFSSYGMHWVRQAPGKLEWVAVIWIWYDGSNKYYADSVKGRFTI
SRDNSKNTLYLQMNSLRAEDTAVYYCARRGGIVVAAPFDYWGGTLTVSS (SEQ ID NO: 5);
QVQLVESGGGVVQPGRLRLSCEASGITFRNYGMHWVRQAPGKLEWVAVMWYDGSNKYYADSVKGRF
TISRDNKNTVYLQMNSLRAEDTAVYYCARRGHIATAAPFDYWGGTLTVSS (SEQ ID NO: 6);
- 15 QVQLVESGGGVVQPGRLRLSCTASGFTFRSYGMHWVRQAPGKLEWVSVIWIWYDGNNIYYADSVKGRFTIS
RDNSKNTLYLQMDSLRAEDTAVYYCARRLAITSAPFDYWGGTLTVSS (SEQ ID NO: 7);

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- QVQLVQSGAEVKKPGASVKVSCKASGYAFTTYGITWVRQAPGQGLEWMGWISAYNGNTNYAEKVQGRFT
 MTTDTSTNTAYMELRSLRSDDTAVYFCARKGHYSGTYYNPFGDFWQGQTMVTVSS (SEQ ID NO: 8);
 EVQLVESGGGLVQPGGSLKLSCTASGLTSLDSAMHWVRQASGKGLEWVGRIRNKANRYATEYAASVKGRF
 TISRDDSKNTAYLQMNSLKTEDTAVYYCTRNWKIFLDYWGQGTSLTVTVSS (SEQ ID NO: 9);
- 5 EVQLLESGGGLVQPGGSLRLSCAASGFTFNNGMSWVRQGPQGKLEWVSSISGSGGTTFYADSVKGRFTIS
 RDNSKNTLYLQMNSLRAEDTAVYYCGKGGYCSSSGCRHYGMDVWGQGTSLTVTVSS (SEQ ID NO: 10);
 EVQLVESGGNLVQPGGSLRLSCAASGFTFTSHAMNHWVRQAPGKLEWVSVITGRGFDTHYADSVKGRFTIS
 RDISKNTLYLQMNSLRAEDTAVYYCAKGLYDSGNYIDYWGQGTSLTVTVSS (SEQ ID NO: 11);
 QVQLVQSGAEVKKPGASVKVSCKASGYAFTTYGITWVRQAPGQGLEWMGWISAYNGNTNYAEKVQGRFT
- 10 MTTDTSTNTAYMELRSLRSDDTAVYFCARKGHYSGTYYNPFGDFWQGQTMVTVSS (SEQ ID NO: 12).
HCDR1 Amino Acid Sequences:
 GITFRNYG (SEQ ID NO: 13); GGSFSGYY (SEQ ID NO: 14); GFTFSTYG (SEQ ID NO: 15); GDSINYY
 (SEQ ID NO: 16); GFTFSSYG (SEQ ID NO: 17); GITFRNYG (SEQ ID NO: 18); GFTFRSYG (SEQ ID NO:
 19); GYAFTTYG (SEQ ID NO: 20); GLTSLDSA (SEQ ID NO: 21); GFTFNNGY (SEQ ID NO: 22);
- 15 GFTFTSHA (SEQ ID NO: 23); GYAFTTYG (SEQ ID NO: 24).
HCDR2 Amino Acid Sequences:
 MWYDGSNK (SEQ ID NO: 25); ILHSGRT (SEQ ID NO: 26); IWHDGSDK (SEQ ID NO: 27); IYSGSA
 (SEQ ID NO: 28); IWIDGSNK (SEQ ID NO: 29); MWYDGSN (SEQ ID NO: 30); IWIDGNNI (SEQ ID NO:
 31); ISAYNGN (SEQ ID NO: 32); IRNKANRYAT (SEQ ID NO: 33); SGSGGT (SEQ ID NO: 34); ITGRGFD
 T (SEQ ID NO: 35); ISAYNGNT (SEQ ID NO: 36).
- 20 *HCDR3 Amino Acid Sequences:*
 ARRGTIRTAAPFDY (SEQ ID NO: 37); AGRIAARHGWFDY (SEQ ID NO: 38); ARRGRGTVFDH (SEQ ID
 NO: 39); ARGAVKYFRH (SEQ ID NO: 40); ARRGIVVAAPFDY (SEQ ID NO: 41); ARRGHIAAPFD
 (SEQ ID NO: 42); ARRLAITSAPFDY (SEQ ID NO: 43); CARKGHYSGTYYNPFGFD (SEQ ID NO: 44);
- 25 TRNWKIFLDY (SEQ ID NO: 45); CGKGGYCSSSGCRH (SEQ ID NO: 46); AKGLYDSGNYIDY (SEQ ID
 NO: 47); ARKGHYSGTYYNPFGFD (SEQ ID NO: 48).
HC Amino Acid Sequence:
 QVQLVESGGGVVQPGRLSLCTASGITFRNYGMHWVRQAPGKLEWVAVMWYDGSNKYYADSVKGRF
 TISGDNKSVYLQMNSLRAEDTAVYYCARRGTIRTAAPFDYWGQGTSLTVTVSSASTKGPSVFPLAPCSRSTSEST
 30 AALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDPKPSNTKVD
 KRVESKYGPPCPPAPGGGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNA
 KTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTKAKGQPREPQVYTLPPSQEEMTK

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- NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEA
LHNHYTQKSLSLGLK (SEQ ID NO: 97) *underlined and bolded asparagine (N) may be mutated to
a glutamine (Q) for conjugation by transglutaminase;
- QVQLQQWGAGLLKPSATLSRTCAYVGGSFSGYYWNWIRQSPGKGLEWIGELHSGRTNYPNPSLKSRTISV
5 DTSKNQFSLKLTSVTAADTAVYYCAGRIARHGWFDPWGQGTLLTVSSASTKGPSVFPLAPCSRSTSESTAAL
GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTPSSSLGKTYTCNVDHKPSNTKVDKRV
ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTK
PREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ
VSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHN
10 HYTQKSLSLGLK (SEQ ID NO: 98) *underlined and bolded asparagine (N) may be mutated to a
glutamine (Q) for conjugation by transglutaminase;
- QVQLVESGGGVVQPGSRSLRSCAASGFTSTYGMHWVRQAPGKGLEWVAVIWHGSDKYYVDSVKGRFS
IARDNSKNTLYLQMNSLRVEDTGIYYCARRGIRGTVFDHWGLGLTLTVSSASTKGPSVFPLAPCSRSTSESTA
LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTPSSSLGKTYTCNVDHKPSNTKVDKR
15 VESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKT
KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKN
QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALH
NHYTQKSLSLGLK (SEQ ID NO: 99) *underlined and bolded asparagine (N) may be mutated to a
glutamine (Q) for conjugation by transglutaminase;
- 20 QVQLQESGPGLVKPSSETLSLTCTVSGDSINNYWTWLRQPPGKLEWIGIYYSGSANYNP SLKSRTISVDT
SKNQFSLKLTNSVTAADTAVYYCARGAVKYFRHWGQGTLLTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVK
DYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTPSSSLGKTYTCNVDHKPSNTKVDKRVESKYG
PPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQ
FNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCL
25 VKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQK
SLSLGLK (SEQ ID NO: 100) *underlined and bolded asparagine (N) may be mutated to a
glutamine (Q) for conjugation by transglutaminase;
- QVQLVESGGGVVQPGTSLRSLSCAASGFTSSYGMHWVRQAPGKLEWVAVIWIWIDGSNKYYADSVKGRFTI
SRDNSKNTLYLQMNSLRAEDTAVYYCARRGIVVAAPFDYWGQGTLLTVSSASTKGPSVFPLAPCSRSTSES
30 TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTPSSSLGKTYTCNVDHKPSNTKV
DKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHN
AKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMT

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- KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHE
ALHNHYTQKSLSLGLK (SEQ ID NO: 101) *underlined and bolded asparagine (N) may be mutated
to a glutamine (Q) for conjugation by transglutaminase;
QVQLVESGGGVVQPGSRSLRSCTASGFTFRSYGMHWVRQAPGKGLEWVSVIWDGNNIYADSVKGRFTIS
5 RDNSKNTLYLQMDSLR AEDTAVYYCARRLAITS AAPFDYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSESTA
ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKV D K
RVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAK
TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKN
QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALH
10 NHYTQKSLSLGLK (SEQ ID NO: 102) *underlined and bolded asparagine (N) may be mutated to a
glutamine (Q) for conjugation by transglutaminase;
EVQLVESGGNLVQPGGSLRLS CAASGFTFTSHAMNWVRQAPGKGLEWVSVITGRGFDTHYADSVKGRFTIS
RDISKNTLYLQMNSLR AEDTAVYYCAKGLYDSGNYIDYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSESTA
ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKV D K
15 RVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAK
TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKN
QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALH
NHYTQKSLSLGLK (SEQ ID NO: 103) *underlined and bolded asparagine (N) may be mutated to a
glutamine (Q) for conjugation by transglutaminase;
20 QVQLVESGGGVVQPGSRSLRSCEASGITFRNYGMHWVRQAPGKGLEWVAVMWYDGSNKYYADSVKGRF
TISRDN SKNTVYLQMNSLR AEDTAVYYCARRGHIATAAPFDYWGQGLTVTVSSAKTTAPSVYPLAPVCGD TT
GSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKV
DKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKDVLMI SLSPIVTCVVDVSEDDPDVQISW FVN NVEVH
TAQTQTHREDYNSTLRVVSALPIQH QDWMSGKEFKCKVNNKDLPAPIERTISKPKG SVRAPQVYVLPPEEE
25 MTKKQVTLTCMVTD FMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSV
VHEGLHNHHTTKSFSRTPGK (SEQ ID NO: 104);
QVQLVQSGAEVKKPGASVKVSCKASGYAFTTYGITWVRQAPGQGLEWMGWISAYNGNTNYAEKVQGRFT
MTTDTSTNTAYMELRSLRSDDTAVYFCARKGHYSGTYNPF GDFW GQGMVTVSSAKTTPPSVYPLAPG
SAAQTNSMVTLGCLVKGYFPEPVTVTVNSGSLSSGVHTFPAVLQSDLYTLSSSVTVPSSTW PSETVTCNVAH
30 PASSTKVDKKIVPRDCGCKPCICTVPEVSSVFIFPPKPKDVLITITLPKVTCVVDISKDDPEVQFSWFVDDDEV
HTAQTQPREEQFNSTFRSVSELPIMHQDWLNGKEFKCRVNSAAFPAPIEKTISKTKGRPKAPQVYTIPPPKEQ

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- MAKDKVSLTCMITDFFPEDITVEWQWNGQPAENYKNTQPIMDTDGSYFVYSKLNQKSNWEAGNTFTCS
VLHEGLHNHHTEKSLSHSPGK (SEQ ID NO: 105);
- EVQLVESGGGLVQPGGSLKLSCTASGLTSDSAMHWVRQASGKGLEWVGRIRNKANRYATEYAASVKGRF
TISRDDSKNTAYLQMNSLKTEDTAVYYCTRNWKIFLFDYWGGQTLTVSSASTKGPSVFPLAPCSRSTSESTA
5 ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDHKPSNTKVDK
RVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAK
TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKN
QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALH
NHYTQKSLSLGK (SEQ ID NO: 106);
- 10 EVQLLESGGGLVQPGGSLRLSCAASGFTFNNGMSWVRQGPQKGLEWVSSISGSGGTTFYADSVKGRFTIS
RDNSKNTLYLQMNSLRAEDTAVYYCGKGGYCSSSGCRHYGMDVWGQGTITVSSAKTTAPSVYPLAPVCG
DTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASS
TKVDKKIEPRGPTIKCPPCKCPAPNLLGGPSVFIFPPKIKDVLMSLSPIVTCVVVDVSEDDPDVQISWVFN
EVHTAQTQTHREDYNSTLRVVSALPIQHQQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVYVLP
15 EEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTPEVLDSGSYFMYSKLRVEKKNWVERNSYS
CSVVHEGLHNHHHTKSFSRTPGK (SEQ ID NO: 107);
- QVQLVQSGAEVKKPGASVKVSCKASGYAFTTYGITWVRQAPGQGLEWMGWISAYNGNTNYAEKVQGRFT
MTTDTSTNTAYMELRSLRSDDTAVYFCARKGHYSGTYYPFGFDWGGQTMVTVSSASTKGPSVFPLAPC
SRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV
20 PSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQFNWYVD
GVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPP
SQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSC
SVMHEALHNHYTQKSLSLGK (SEQ ID NO: 108).

LCVR Amino Acid Sequences:

- 25 DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLT
SSLQPEDFATYYCQSYSTPPITFGQGTRLEIK (SEQ ID NO: 49);
- DIQMTQSPSSVSTSVGDRVTISCRASQDIRKWLAWYQQKPGKAPKLLIYATSSLQSGVPSRFSGSGSGTDFTL
TISSLQPEDFATYFCQQANSFPFTFGQGTKLEIK (SEQ ID NO: 50);
- DIQMTQSPSTLSASVGDRVTLTCRASQSIKSLAWYQQKPGKAPNLLIYKASNLESGVPSRFSGSGSGTEFTLT
30 ISSLQPDDEFATYYCQYNSYSWTFGQGTKVEIK (SEQ ID NO: 51);
- EIVLTQSPGTLSLSPGERATLSCRASQTINHNLAWYQQRPGQAPRLLIYGASNRATAIPDRFSGSGSGTDFTL
TISRLEPEDFEVYSCQYGSPLTFGGGKVEIK (SEQ ID NO: 52);

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- DIQMTQSPSSLSASVGDRTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLT
SSLQPEDFATYYCQQSYSTPPITFGQGTRLEIK (SEQ ID NO: 53);
- DIQMTQSPSSLSASVGDRTISCRASQSISSYLNWYQQKPGKAPKVLMYAASSLQSGVPSRFSGSGSGTDFTL
TISLQPEDFATYYCQQSYSTPPITFGQGTRLEIK (SEQ ID NO: 54);
- 5 DIQMTQSPSSLSASVGDRTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLT
SSLQPEDFATYYCQQSYSTPPITFGQGTRLEIK (SEQ ID NO: 55);
- EIMLMQSPGTLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYGASSRATDIPDRFSGSGSGTDFTL
TISRLEPEDFAVYFCQQYYGSPWTFGQGTKVEIK (SEQ ID NO: 56);
- EIVLTQSPGTLTSPGERATLSCRASQSVGSKYLAWFQQKRGQAPRLLIYGASSRTSGIPDRISGSGSGTDFTLT
10 ISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIK (SEQ ID NO: 57);
- QSVLTQPPSASGTPGQRTVITSCGSSSNIGNNNYIYWYQRLPGTTPKLLIYRNNQRPSGVPDRFSGSKSGTSASL
AISGLRSEDEADYYCAAWDDTLSGYVFGTGKVTVL (SEQ ID NO: 58);
- QSVLTQPPSVSAAPGQKVTISCSGSSSNIGNNNYVSWYQQLPGTAPKLLIYDNNKRPSGIPDRFSGSKSGTSATL
GITGLQTGDEADYYCGTWDLSLFSFNWVFGGGTKLTVL (SEQ ID NO: 59);
- 15 EIVLTQSPGTLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLT
ISRLEPEDFALYFCQQYYGSPWTFGQGTKVEIK (SEQ ID NO: 60).

LCDR1 Amino Acid Sequences:

- QSISSY (SEQ ID NO: 61); QDIRKW (SEQ ID NO: 62); QSISSY (SEQ ID NO: 63); QTINHNN (SEQ ID
NO: 64); QSISSY (SEQ ID NO: 65); QSISSY (SEQ ID NO: 66); QSISSY (SEQ ID NO: 67); QSVSSSY (SEQ
20 ID NO: 68); QSVGSKY (SEQ ID NO: 69); SSNIGNNY (SEQ ID NO: 70); SSNIGNNY (SEQ ID NO: 71);
QSVSSSY (SEQ ID NO: 72).

LCDR2 Amino Acid Sequence:

- AAS (SEQ ID NO: 73); ATS (SEQ ID NO: 74); KAS (SEQ ID NO: 75); GAS (SEQ ID NO: 76); AAS (SEQ ID
NO: 77); AAS (SEQ ID NO: 78); AAS (SEQ ID NO: 79); GA (SEQ ID NO: 80); GAS (SEQ ID NO: 81); RN
25 (SEQ ID NO: 82); DNN (SEQ ID NO: 83); GAS (SEQ ID NO: 84).

LCDR3 Amino Acid Sequence:

- QQSYSTPPIT (SEQ ID NO: 85); QQANSFPFT (SEQ ID NO: 86); QQYNSYSWT (SEQ ID NO: 87);
QQYGSLPLT (SEQ ID NO: 88); QQSYSTPPIT (SEQ ID NO: 89); QSYSTPPIT (SEQ ID NO: 90);
QSYSTPPIT (SEQ ID NO: 91); CQQYYGSPW (SEQ ID NO: 92); QQYGSSPWT (SEQ ID NO: 93);
30 CAAWDDTLSGY (SEQ ID NO: 94); GTWDLSLFSFNWV (SEQ ID NO: 95); QQYYGSPWT (SEQ ID NO:
96).

LC Amino Acid Sequence:

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- DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCQQSYSTPPITFGQGTRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQW
KVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID
NO: 109);
- 5 DIQMTQSPSSVSTSVGDRVTISCRASQDIRKWLA WYQQKPGKAPKLLIYATSSLQSGVPSRFSGSGSGTDFTL
TISSLQPEDFATYFCQQANSFPFTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ
WKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ
ID NO: 110);
- DIQMTQSPSTLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPNLLIYKASNLESGVPSRFSGSGSGTEFTLT
10 ISSLQPDDEFATYYCQQYNSYSWTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ
WKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ
ID NO: 111);
- EIVLTQSPGTLSTLSPGERATLSCRASQTINHNLA WYQQRPGQAPRLLIYGASNRATAIPDRFSGSGSGTDFTL
TISRLEPEDFEVYSCQQYGSLPLTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ
15 WKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ
ID NO: 112);
- DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCQQSYSTPPITFGQGTRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQW
KVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID
20 NO: 113);
- DIQMTQSPSSLSASVGDRVTISCRASQSISSYLNWYQQKPGKAPKVL MYAASSLQSGVPSRFSGSGSGTDFTL
TISSLQPEDFATYYCQQSYSTPPITFGQGTRLEIKRADAAPT VSI FPPSSEQLTSGGASVVCFLNNFYPKDINVK
WKIDGSERQNGVLNSWTDQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ
ID NO: 114);
- 25 DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCQQSYSTPPITFGQGTRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQW
KVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID
NO: 115);
- EIMLMQSPGTLSTLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYGASSRATDIPDRFSGSGSGTDFTL
30 TISRLEPEDFAVYFCQQYGGSPWTFGQGTKEIKRADAAPT VSI FPPSSEQLTSGGASVVCFLNNFYPKDINVK
WKIDGSERQNGVLNSWTDQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ
ID NO: 116);

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EIVLTQSPGTLTLSPGERATLSCRASQSVGSKYLAWFQQKRGQAPRLIYGASSRTSGIPDRISGSGSGTDFTLT
 ISRLEPEDFAVYYCQYGGSPWTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYFPREAKVQ
 WKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ
 ID NO: 117);

5 QSVLTQPPSASGTPGQRTVISCSSNIGNNNYIYQRLPGTTPKLLIYRNNQRPSGVPDRFSGSKSGTSASL
 AISGLRSEDEADYYCAAWDDTLSGYVFGTGKVTVLRAADAAPTIVSIFPPSDEQLTSGGASVVCFLNNFYPKDIN
 VKWKIDGSRQNGVLNSWTDQDSKDYSLSTLTLTDEYERHNSYTCEATHKTSTSPIVKSFNRGEC
 (SEQ ID NO: 118);

QSVLTQPPSVSAAPGQKVTISCSSNIGNNNYVSWYQQLPGTAPKLLIYDNNKRPSGIPDRFSGSKSGTSATL
 10 GITGLQTGDEADYYCGTWDLSLFWVFGGGTKTLTVLQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPG
 AVTVAWKADSSPVKAGVETTPSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
 (SEQ ID NO: 119);

EIVLTQSPGTLTLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLIYGASSRATGIPDRFSGSGSGTDFTLT
 ISRLEPEDFALYFCQYYGSPWTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYFPREAKVQ
 15 WKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ
 ID NO: 120).

In some embodiments described herein, administration of the FNIP1 inhibitor and/or
 FLCN inhibitor can be targeted to adipose tissue or adipose cells. In some embodiments, an
 adipose-specific FNIP1 siRNA can be used to promote lipid oxidation in white adipose tissue
 20 (WAT) for treatment. In some embodiments, the FNIP1 inhibitor and/or FLCN inhibitor can be
 injected into adipose tissue. In some embodiments, the adipose-specific FNIP1 siRNA and/or
 FLCN siRNA can be delivered to adipocytes by using lipid-based transfection reagents for siRNA
 transfection of mature white adipocyte, according to the reverse transfection protocol reported
 by Isidor et al., *Adipocyte*, 2016, 5, 175-185. Essentially, lipofection-based reverse siRNA
 25 transfection reported therein may effectively silence FNIP1 and/or FLCN in mature adipocyte of
 various origins. In some embodiments, the adipose specific FNIP1 siRNA and/or FLCN siRNA can
 be delivered to adipose tissue by adhering to the proposed "gold standard" illustrated in the
 published article by Romanelli et al., *Diabetes*, 2020, 69, 2581-2588, with proper adaption. The
 siRNA against FNIP1 or FLCN can be transferred via viral or non-viral vectors. Adipocyte-specific
 30 antibodies against adipocyte-selective targets such as the amino acid transporter ASC-1 or the
 the brown cell surface markers to improve tropism are contemplated.

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Antigen-binding fragment include, but are not limited to, a monovalent Fab', a divalent Fab2, a F(ab)'3 fragment, a single-chain fragment variable (scFv), a bis-scFv, a (scFv)2, a diabody, a minibody, a nanobody, a triabody, a tetrabody, a disulfide stabilized Fv protein (dsFv), a single-domain antibody (sdAb), an Ig NAR, a bispecific antibody or binding fragment thereof, a bi-specific T-cell engager (BiTE), a trispecific antibody, and chemically modified derivatives thereof.

A bifunctional linker such as, for example, M3463 (purchased from Broadpharm, BP-22617) can be used as a linker to join the siRNA or antisense molecule to the antibody. The modified single strands can be synthesized by standard automated oligonucleotide synthesis. During the on-bead synthesis, a 5' sense strand modification with a six carbon chain terminating with a primary amino group can be attached to the abasic group to provide a handle for the linker. Standard deprotection and cleavage of the strands followed by reverse phase high-performance liquid chromatography (HPLC) purification furnished the strands that can be annealed to form the duplex siRNA. The bifunctional linker (such as, for example, M3463) can be coupled to the terminal amino group of the 5' sense strand modification using an excess of the linker. The mixture can then be purified by reverse phase HPLC to furnish the functionalized duplex siRNA ready for antibody conjugation. To conjugate the siRNA to the antibody, the antibody can be treated with 1 mM dithiothreitol or TCEP (tris(2-carboxyethyl)phosphine) at 37°C for 30 minutes. After gel filtration (G-25, pH 4.5 sodium acetate), the bis-maleimido linker siRNA can be added to the reduced antibody and the mixture can be adjusted to pH 7.0 with 1 M HEPES (pH 7.4). After 1 hour, the conjugates can be purified by size exclusion chromatography and sterile filtered. Protein and linker payload concentrations can be determined by UV spectral analysis. Size-exclusion HPLC can be used to establish that the conjugates used are >95% monomeric, and reversed-phase high-performance liquid chromatography (RP-HPLC) can be used to establish that there is <0.5% unconjugated linker payload. UV (Hamblett et al., Cancer Res., 2004, 10, 7063) and hydrophobic interaction chromatography (HIC) can be used to determine the loadings to be 1-1.6 siRNAs/antibody.

The present disclosure also provides methods of identifying a subject having an increased risk of developing muscle disorder. In some embodiments, the method comprises determining or having determined in a biological sample obtained from the subject the presence or absence of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule (such as a genomic nucleic acid molecule, mRNA molecule, and/or cDNA

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molecule). When the subject lacks an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule (i.e., the subject is genotypically categorized as FNIP1 reference and/or FLCN reference), then the subject has an increased risk of developing muscle disorder. When the subject has an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule (i.e., the subject is heterozygous or homozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule), then the subject has a decreased risk of developing muscle disorder. In some embodiments, the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule is an FNIP1 variant genomic nucleic acid molecule or an FLCN variant genomic nucleic acid molecule that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule.

Having a single copy of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule is more protective of a subject from developing muscle disorder than having no copies of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule. Without intending to be limited to any particular theory or mechanism of action, it is believed that a single copy of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule (i.e., heterozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule) is protective of a subject from developing muscle disorder and it is also believed that having two copies of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule (i.e., homozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule) may be more protective of a subject from developing muscle disorder, relative to a subject with a single copy. Thus, in some embodiments, a single copy of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule may not be completely protective, but instead, may be partially or incompletely protective of a subject from developing muscle disorder. While not desiring to be bound by any particular theory, there may be additional factors or molecules involved in the development of muscle disorder that are still present in a subject having a single copy of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, thus resulting in less than complete protection from the development of muscle disorder.

Determining whether a subject has an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule in a biological sample from a subject and/or determining whether a subject has an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic

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acid molecule can be carried out by any of the methods described herein. In some embodiments, these methods can be carried out *in vitro*. In some embodiments, these methods can be carried out *in situ*. In some embodiments, these methods can be carried out *in vivo*. In any of these embodiments, the nucleic acid molecule can be present within a cell

5 obtained from the subject.

In some embodiments, when a subject is identified as having an increased risk of developing muscle disorder, the subject is administered a muscle disorder therapeutic agent and/or an FNIP1 inhibitor and/or an FLCN inhibitor, as described herein. For example, when the subject is FNIP1 reference and/or FLCN reference, and therefore has an increased risk of developing muscle disorder, the subject is administered a muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and/or is administered an FNIP1 inhibitor and/or an FLCN inhibitor. In some embodiments, when the subject is heterozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, the subject is administered the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and/or is administered an FNIP1 inhibitor and/or an FLCN inhibitor. In some embodiments, when the subject is homozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, the subject is administered a muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount. In some embodiments, the subject is FNIP1 reference and/or FLCN reference. In some embodiments, the subject is heterozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule. In some embodiments, the subject is homozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule.

The present disclosure also provides methods of determining a subject's aggregate burden, or risk score, of having two or more FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecules, and/or two or more FNIP1 variant polypeptides or two or more FLCN variant polypeptides associated with a decreased risk of developing muscle disorder. The aggregate burden is the sum of two or more genetic variants that can be carried out in an association analysis with muscle disorder. In some embodiments, the subject is homozygous for one or more FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecules associated with a decreased risk of developing muscle disorder. In some embodiments, the subject is heterozygous for one or more FNIP1 variant nucleic acid molecule

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and/or an FLCN variant nucleic acid molecules associated with a decreased risk of developing muscle disorder. When the subject has a lower aggregate burden, the subject has an increased risk of developing muscle disorder, and the subject is administered or continued to be administered the muscle disorder therapeutic agent in an amount that is the same as or less than the standard dosage amount, and/or an FNIP1 inhibitor and/or an FLCN inhibitor. When the subject has a higher aggregate burden, the subject has a decreased risk of developing muscle disorder and the subject is administered or continued to be administered the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount. The higher the aggregate burden, the lower the risk of developing muscle disorder.

10 In some embodiments, a subject's aggregate burden of having any two or more FNIP1 variant nucleic acid molecules and/or any two or more FLCN variant nucleic acid molecules represents a weighted sum of a plurality of any of the FNIP1 variant nucleic acid molecules and/or any of the FLCN variant nucleic acid molecules. In some embodiments, the aggregate burden is calculated using at least about 2, at least about 3, at least about 4, at least about 5, at least about 10, at least about 20, at least about 30, at least about 40, at least about 50, at least about 60, at least about 70, at least about 80, at least about 100, at least about 120, at least about 150, at least about 200, at least about 250, at least about 300, at least about 400, at least about 500, at least about 1,000, at least about 10,000, at least about 100,000, or at least about or more than 1,000,000 genetic variants present in or around (up to 10 Mb) the FNIP1 gene or FLCN gene, where the genetic burden is the number of alleles multiplied by the association estimate with muscle disorder or related outcome for each allele (e.g., a weighted polygenic burden score). In some embodiments, when the subject has an aggregate burden higher than a desired threshold score, the subject has a decreased risk of developing muscle disorder. In some embodiments, when the subject has an aggregate burden lower than a desired threshold score, the subject has an increased risk of developing muscle disorder.

25 In some embodiments, the aggregate burden may be divided into quintiles, e.g., top quintile, second quintile, intermediate quintile, fourth quintile, and bottom quintile, wherein the top quintile of aggregate burden corresponds to the lowest risk group and the bottom quintile of aggregate burden corresponds to the highest risk group. In some embodiments, a subject having a higher aggregate burden comprises the highest weighted aggregate burdens, including, but not limited to the top 10%, top 20%, top 30%, top 40%, or top 50% of aggregate burdens from a subject population. In some embodiments, the genetic variants comprise the

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genetic variants having association with muscle disorder in the top 10%, top 20%, top 30%, top 40%, or top 50% of p-value range for the association. In some embodiments, each of the identified genetic variants comprise the genetic variants having association with muscle disorder with p-value of no more than about 10^{-2} , about 10^{-3} , about 10^{-4} , about 10^{-5} , about 10^{-6} , about 10^{-7} , about 10^{-8} , about 10^{-9} , about 10^{-10} , about 10^{-11} , about 10^{-12} , about 10^{-13} , about 10^{-14} , about or 10^{-15} . In some embodiments, the identified genetic variants comprise the genetic variants having association with muscle disorder with p-value of less than 5×10^{-8} . In some embodiments, the identified genetic variants comprise genetic variants having association with muscle disorder in high-risk subjects as compared to the rest of the reference population with odds ratio (OR) about 1.5 or greater, about 1.75 or greater, about 2.0 or greater, or about 2.25 or greater for the top 20% of the distribution; or about 1.5 or greater, about 1.75 or greater, about 2.0 or greater, about 2.25 or greater, about 2.5 or greater, or about 2.75 or greater. In some embodiments, the odds ratio (OR) may range from about 1.0 to about 1.5, from about 1.5 to about 2.0, from about 2.0 to about 2.5, from about 2.5 to about 3.0, from about 3.0 to about 3.5, from about 3.5 to about 4.0, from about 4.0 to about 4.5, from about 4.5 to about 5.0, from about 5.0 to about 5.5, from about 5.5 to about 6.0, from about 6.0 to about 6.5, from about 6.5 to about 7.0, or greater than 7.0. In some embodiments, high-risk subjects have aggregate burdens in the bottom decile, quintile, or tertile in a reference population. The threshold of the aggregate burden can be determined on the basis of the nature of the intended practical application and the risk difference that would be considered meaningful for that practical application.

In embodiments where the aggregate burden is determined for FNIP1 genetic variants and/or FLCN genetic variants associated with muscle disorder, then the aggregate burden represents a subject's risk score for developing muscle disorder. In some embodiments, the aggregate burden or risk score includes the FNIP1 variant genomic nucleic acid molecule and/or FLCN variant genomic nucleic acid molecule that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule. In some embodiments, a subject's aggregate burden can be determined for FNIP1 genetic variants and/or FLCN genetic variants associated with muscle disorder in combination with additional genetic variants for other genes also associated with muscle disorder to produce a polygenic risk score (PRS) for developing muscle disorder. In some embodiments, the PRS includes the FNIP1 variant genomic nucleic acid

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molecule and/or FLCN variant genomic nucleic acid molecule that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule.

5 The present disclosure also provides methods of detecting the presence or absence of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule (i.e., a genomic nucleic acid molecule, an mRNA molecule, or a cDNA molecule produced from an mRNA molecule) in a biological sample from a subject. It is understood that gene sequences within a population and mRNA molecules encoded by such genes can vary due to polymorphisms such as single-nucleotide polymorphisms.

10 The biological sample can be derived from any cell, tissue, or biological fluid from the subject. The biological sample may comprise any clinically relevant tissue, such as a bone marrow sample, a tumor biopsy, a fine needle aspirate, or a sample of bodily fluid, such as blood, gingival crevicular fluid, plasma, serum, lymph, ascitic fluid, cystic fluid, or urine. In some cases, the sample comprises a buccal swab. The biological sample used in the methods
15 disclosed herein can vary based on the assay format, nature of the detection method, and the tissues, cells, or extracts that are used as the sample. A biological sample can be processed differently depending on the assay being employed. For example, when detecting any FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, preliminary processing designed to isolate or enrich the biological sample for the genomic DNA can be
20 employed. A variety of techniques may be used for this purpose. When detecting the level of any FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, different techniques can be used to enrich the biological sample with mRNA molecules. Various methods to detect the presence or level of an mRNA molecule or the presence of a particular variant genomic DNA locus can be used.

25 In some embodiments, detecting an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule in a subject comprises performing a sequence analysis on a biological sample obtained from the subject to determine whether an FNIP1 genomic nucleic acid molecule and/or FLCN genomic nucleic acid molecule in the biological sample, and/or an FNIP1 mRNA molecule and/or FLCN mRNA molecule in the biological sample, and/or an FNIP1
30 cDNA molecule and/or FLCN cDNA molecule produced from an mRNA molecule in the biological sample, is present in the sample. In some embodiments, the methods detect the FNIP1 variant genomic nucleic acid molecule and/or FLCN variant genomic nucleic acid molecule that

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comprises any one or more of the genetic variations described herein, or an mRNA molecule produced therefrom, or a cDNA molecule produced from the mRNA molecule.

In some embodiments, the methods of detecting the presence or absence of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule (such as, for example, a genomic nucleic acid molecule, an mRNA molecule, and/or a cDNA molecule produced from an mRNA molecule) in a subject comprise performing an assay on a biological sample obtained from the subject. The assay determines whether a nucleic acid molecule in the biological sample comprises a particular nucleotide sequence.

In some embodiments, the biological sample comprises a cell or cell lysate. Such methods can further comprise, for example, obtaining a biological sample from the subject comprising an FNIP1 genomic nucleic acid molecule or mRNA molecule and/or FLCN genomic nucleic acid molecule or mRNA molecule, and if mRNA, optionally reverse transcribing the mRNA into cDNA. Such assays can comprise, for example determining the identity of these positions of the particular FNIP1 nucleic acid molecule and/or FLCN nucleic acid molecule. In some embodiments, the method is an *in vitro* method.

In some embodiments, the determining step, detecting step, or sequence analysis comprises sequencing at least a portion of the nucleotide sequence of the FNIP1 genomic nucleic acid molecule and/or FLCN genomic nucleic acid molecule, the FNIP1 mRNA molecule and/or FLCN mRNA molecule, or the FNIP1 cDNA molecule and/or FLCN cDNA molecule in the biological sample that comprises a genetic variation compared to the corresponding FNIP1 reference molecule and/or FLCN reference molecule. In some embodiments, the sequenced portion comprises one or more variations that cause a loss-of-function (partial or complete) or are predicted to cause a loss-of-function (partial or complete).

In some embodiments, the assay comprises sequencing the entire nucleic acid molecule. In some embodiments, only an FNIP1 genomic nucleic acid molecule and/or FNIP1 genomic nucleic acid molecule is analyzed. In some embodiments, only an FNIP1 mRNA and/or FLCN mRNA is analyzed. In some embodiments, only an FNIP1 cDNA obtained from the FNIP1 mRNA and/or FLCN cDNA obtained from the FLCN mRNA is analyzed.

Alteration-specific polymerase chain reaction techniques can be used to detect mutations such as SNPs in a nucleic acid sequence. Alteration-specific primers can be used because the DNA polymerase will not extend when a mismatch with the template is present.

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In some embodiments, the nucleic acid molecule in the sample is mRNA and the mRNA is reverse-transcribed into a cDNA prior to the amplifying step. In some embodiments, the nucleic acid molecule is present within a cell obtained from the subject.

In some embodiments, the assay comprises contacting the biological sample with a
5 primer or probe, such as an alteration-specific primer or alteration-specific probe, that specifically hybridizes to an FNIP1 variant genomic sequence, variant mRNA sequence, or variant cDNA sequence and not the corresponding FNIP1 reference sequence under stringent conditions and determining whether hybridization has occurred and/or contacting the
10 biological sample with a primer or probe, such as an alteration-specific primer or alteration-specific probe, that specifically hybridizes to an FLCN variant genomic sequence, variant mRNA sequence, or variant cDNA sequence and not the corresponding FLCN reference sequence under stringent conditions and determining whether hybridization has occurred.

In some embodiments, the determining step, detecting step, or sequence analysis comprises: a) amplifying at least a portion of the FNIP1 nucleic acid molecule that encodes the
15 FNIP1 polypeptide and/or amplifying at least a portion of the FLCN nucleic acid molecule that encodes the FLCN polypeptide; b) labeling the amplified nucleic acid molecule with a detectable label; c) contacting the labeled nucleic acid molecule with a support comprising an alteration-specific probe; and d) detecting the detectable label.

In some embodiments, the assay comprises RNA sequencing (RNA-Seq). In some
20 embodiments, the assays also comprise reverse transcribing mRNA into cDNA, such as by the reverse transcriptase polymerase chain reaction (RT-PCR).

In some embodiments, the methods utilize probes and primers of sufficient nucleotide length to bind to the target nucleotide sequence and specifically detect and/or identify a polynucleotide comprising an FNIP1 variant genomic nucleic acid molecule, variant mRNA
25 molecule, or variant cDNA molecule or FLCN variant genomic nucleic acid molecule, variant mRNA molecule, or variant cDNA molecule. The hybridization conditions or reaction conditions can be determined by the operator to achieve this result. The nucleotide length may be any length that is sufficient for use in a detection method of choice, including any assay described or exemplified herein. Such probes and primers can hybridize specifically to a target nucleotide
30 sequence under high stringency hybridization conditions. Probes and primers may have complete nucleotide sequence identity of contiguous nucleotides within the target nucleotide sequence, although probes differing from the target nucleotide sequence and that retain the

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ability to specifically detect and/or identify a target nucleotide sequence may be designed by conventional methods. Probes and primers can have about 80%, about 85%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or 100% sequence identity or complementarity with the nucleotide sequence of the target nucleic acid molecule.

Illustrative examples of nucleic acid sequencing techniques include, but are not limited to, chain terminator (Sanger) sequencing and dye terminator sequencing. Other methods involve nucleic acid hybridization methods other than sequencing, including using labeled primers or probes directed against purified DNA, amplified DNA, and fixed cell preparations (fluorescence in situ hybridization (FISH)). In some methods, a target nucleic acid molecule may be amplified prior to or simultaneous with detection. Illustrative examples of nucleic acid amplification techniques include, but are not limited to, polymerase chain reaction (PCR), ligase chain reaction (LCR), strand displacement amplification (SDA), and nucleic acid sequence based amplification (NASBA). Other methods include, but are not limited to, ligase chain reaction, strand displacement amplification, and thermophilic SDA (tSDA).

In hybridization techniques, stringent conditions can be employed such that a probe or primer will specifically hybridize to its target. In some embodiments, a polynucleotide primer or probe under stringent conditions will hybridize to its target sequence to a detectably greater degree than to other non-target sequences, such as, at least 2-fold, at least 3-fold, at least 4-fold, or more over background, including over 10-fold over background. In some embodiments, a polynucleotide primer or probe under stringent conditions will hybridize to its target nucleotide sequence to a detectably greater degree than to other nucleotide sequences by at least 2-fold. In some embodiments, a polynucleotide primer or probe under stringent conditions will hybridize to its target nucleotide sequence to a detectably greater degree than to other nucleotide sequences by at least 3-fold. In some embodiments, a polynucleotide primer or probe under stringent conditions will hybridize to its target nucleotide sequence to a detectably greater degree than to other nucleotide sequences by at least 4-fold. In some embodiments, a polynucleotide primer or probe under stringent conditions will hybridize to its target nucleotide sequence to a detectably greater degree than to other nucleotide sequences by over 10-fold over background. Stringent conditions are sequence-dependent and will be different in different circumstances.

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Appropriate stringency conditions which promote DNA hybridization, for example, 6X sodium chloride/sodium citrate (SSC) at about 45°C., followed by a wash of 2X SSC at 50°C, are known or can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. Typically, stringent conditions for hybridization and detection will be those

5 in which the salt concentration is less than about 1.5 M Na⁺ ion, typically about 0.01 to 1.0 M Na⁺ ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes (such as, for example, 10 to 50 nucleotides) and at least about 60°C for longer probes (such as, for example, greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. Optionally, wash

10 buffers may comprise about 0.1% to about 1% SDS. Duration of hybridization is generally less than about 24 hours, usually about 4 to about 12 hours. The duration of the wash time will be at least a length of time sufficient to reach equilibrium.

In some embodiments, such isolated nucleic acid molecules comprise or consist of at least about 5, at least about 8, at least about 10, at least about 11, at least about 12, at least

15 about 13, at least about 14, at least about 15, at least about 16, at least about 17, at least about 18, at least about 19, at least about 20, at least about 21, at least about 22, at least about 23, at least about 24, at least about 25, at least about 30, at least about 35, at least about 40, at least about 45, at least about 50, at least about 55, at least about 60, at least about 65, at least about 70, at least about 75, at least about 80, at least about 85, at least about 90, at least about 95, at

20 least about 100, at least about 200, at least about 300, at least about 400, at least about 500, at least about 600, at least about 700, at least about 800, at least about 900, at least about 1000, at least about 2000, at least about 3000, at least about 4000, or at least about 5000 nucleotides. In some embodiments, such isolated nucleic acid molecules comprise or consist of at least about 5, at least about 8, at least about 10, at least about 11, at least about 12, at least

25 about 13, at least about 14, at least about 15, at least about 16, at least about 17, at least about 18, at least about 19, at least about 20, at least about 21, at least about 22, at least about 23, at least about 24, or at least about 25 nucleotides. In some embodiments, the isolated nucleic acid molecules comprise or consist of at least about 18 nucleotides. In some embodiments, the isolated nucleic acid molecules comprise or consists of at least about 15 nucleotides. In some

30 embodiments, the isolated nucleic acid molecules consist of or comprise from about 10 to about 35, from about 10 to about 30, from about 10 to about 25, from about 12 to about 30, from about 12 to about 28, from about 12 to about 24, from about 15 to about 30, from about

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15 to about 25, from about 18 to about 30, from about 18 to about 25, from about 18 to about 24, or from about 18 to about 22 nucleotides. In some embodiments, the isolated nucleic acid molecules consist of or comprise from about 18 to about 30 nucleotides. In some
embodiments, the isolated nucleic acid molecules comprise or consist of at least about 15
5 nucleotides to at least about 35 nucleotides.

In some embodiments, such isolated nucleic acid molecules hybridize to FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecules (such as genomic nucleic acid molecules, mRNA molecules, and/or cDNA molecules) under stringent conditions. Such nucleic acid molecules can be used, for example, as probes, primers, alteration-specific probes,
10 or alteration-specific primers as described or exemplified herein, and include, without limitation primers, probes, antisense RNAs, shRNAs, and siRNAs, each of which is described in more detail elsewhere herein and can be used in any of the methods described herein.

In some embodiments, the isolated nucleic acid molecules hybridize to at least about 15 contiguous nucleotides of a nucleic acid molecule that is at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least
15 about 96%, at least about 97%, at least about 98%, at least about 99%, or 100% identical to FNIP1 variant nucleic acid molecule or an FLCN variant nucleic acid molecules. In some embodiments, the isolated nucleic acid molecules consist of or comprise from about 15 to about 100 nucleotides, or from about 15 to about 35 nucleotides. In some embodiments, the
20 isolated nucleic acid molecules consist of or comprise from about 15 to about 100 nucleotides. In some embodiments, the isolated nucleic acid molecules consist of or comprise from about 15 to about 35 nucleotides.

In some embodiments, the alteration-specific probes and alteration-specific primers comprise DNA. In some embodiments, the alteration-specific probes and alteration-specific
25 primers comprise RNA.

In some embodiments, the probes and primers described herein (including alteration-specific probes and alteration-specific primers) have a nucleotide sequence that specifically hybridizes to any of the nucleic acid molecules disclosed herein, or the complement thereof. In some embodiments, the probes and primers specifically hybridize to any of the nucleic acid
30 molecules disclosed herein under stringent conditions.

In some embodiments, the primers, including alteration-specific primers, can be used in second generation sequencing or high throughput sequencing. In some instances, the

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primers, including alteration-specific primers, can be modified. In particular, the primers can comprise various modifications that are used at different steps of, for example, Massive Parallel Signature Sequencing (MPSS), Polony sequencing, and 454 Pyrosequencing. Modified primers can be used at several steps of the process, including biotinylated primers in the cloning step
5 and fluorescently labeled primers used at the bead loading step and detection step. Polony sequencing is generally performed using a paired-end tags library wherein each molecule of DNA template is about 135 bp in length. Biotinylated primers are used at the bead loading step and emulsion PCR. Fluorescently labeled degenerate nonamer oligonucleotides are used at the detection step. An adaptor can contain a 5'-biotin tag for immobilization of the DNA library
10 onto streptavidin-coated beads.

The probes and primers described herein can be used to detect a nucleotide variation within any of the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecules disclosed herein. The primers described herein can be used to amplify any FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, or a fragment
15 thereof.

In the context of the disclosure "specifically hybridizes" means that the probe or primer (such as, for example, the alteration-specific probe or alteration-specific primer) does not hybridize to a nucleic acid sequence encoding an FNIP1 reference genomic nucleic acid molecule, an FNIP1 reference mRNA molecule, and/or an FNIP1 reference cDNA molecule or
20 does not hybridize to a nucleic acid sequence encoding an FLCN reference genomic nucleic acid molecule, an FLCN reference mRNA molecule, and/or an FLCN reference cDNA molecule.

In some embodiments, the probes (such as, for example, an alteration-specific probe) comprise a label. In some embodiments, the label is a fluorescent label, a radiolabel, or biotin.

The present disclosure also provides supports comprising a substrate to which any one
25 or more of the probes disclosed herein is attached. Solid supports are solid-state substrates or supports with which molecules, such as any of the probes disclosed herein, can be associated. A form of solid support is an array. Another form of solid support is an array detector. An array detector is a solid support to which multiple different probes have been coupled in an array, grid, or other organized pattern. A form for a solid-state substrate is a microtiter dish, such as a
30 standard 96-well type. In some embodiments, a multiwell glass slide can be employed that normally contains one array per well.

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The genomic nucleic acid molecules, mRNA molecules, and cDNA molecules can be from any organism. For example, the genomic nucleic acid molecules, mRNA molecules, and cDNA molecules can be human or an ortholog from another organism, such as a non-human mammal, a rodent, a mouse, or a rat. It is understood that gene sequences within a population
5 can vary due to polymorphisms such as single-nucleotide polymorphisms.

Also provided herein are functional polynucleotides that can interact with the disclosed nucleic acid molecules. Examples of functional polynucleotides include, but are not limited to, antisense molecules, aptamers, ribozymes, triplex forming molecules, and external guide sequences. The functional polynucleotides can act as effectors, inhibitors, modulators,
10 and stimulators of a specific activity possessed by a target molecule, or the functional polynucleotides can possess a *de novo* activity independent of any other molecules.

The isolated nucleic acid molecules disclosed herein can comprise RNA, DNA, or both RNA and DNA. The isolated nucleic acid molecules can also be linked or fused to a heterologous nucleic acid sequence, such as in a vector, or a heterologous label. For example, the isolated
15 nucleic acid molecules disclosed herein can be within a vector or as an exogenous donor sequence comprising the isolated nucleic acid molecule and a heterologous nucleic acid sequence. The isolated nucleic acid molecules can also be linked or fused to a heterologous label. The label can be directly detectable (such as, for example, fluorophore) or indirectly detectable (such as, for example, hapten, enzyme, or fluorophore quencher). Such labels can be
20 detectable by spectroscopic, photochemical, biochemical, immunochemical, or chemical means. Such labels include, for example, radiolabels, pigments, dyes, chromogens, spin labels, and fluorescent labels. The label can also be, for example, a chemiluminescent substance; a metal-containing substance; or an enzyme, where there occurs an enzyme-dependent secondary generation of signal. The term "label" can also refer to a "tag" or hapten that can
25 bind selectively to a conjugated molecule such that the conjugated molecule, when added subsequently along with a substrate, is used to generate a detectable signal. For example, biotin can be used as a tag along with an avidin or streptavidin conjugate of horseradish peroxidase (HRP) to bind to the tag, and examined using a calorimetric substrate (such as, for example, tetramethylbenzidine (TMB)) or a fluorogenic substrate to detect the presence of
30 HRP. Exemplary labels that can be used as tags to facilitate purification include, but are not limited to, myc, HA, FLAG or 3XFLAG, 6Xhis or polyhistidine, glutathione-S-transferase (GST), maltose binding protein, an epitope tag, or the Fc portion of immunoglobulin. Numerous labels

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include, for example, particles, fluorophores, haptens, enzymes and their calorimetric, fluorogenic and chemiluminescent substrates and other labels.

Percent identity (or percent complementarity) between particular stretches of nucleotide sequences within nucleic acid molecules or amino acid sequences within polypeptides can be determined routinely using BLAST programs (basic local alignment search tools) and PowerBLAST programs (Altschul *et al.*, J. Mol. Biol., 1990, 215, 403-410; Zhang and Madden, Genome Res., 1997, 7, 649-656) or by using the Gap program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, Madison Wis.), using default settings, which uses the algorithm of Smith and Waterman (Adv. Appl. Math., 1981, 2, 482-489). Herein, if reference is made to percent sequence identity, the higher percentages of sequence identity are preferred over the lower ones.

The present disclosure also provides muscle disorder therapeutic agents that treat, prevent, or inhibit muscle disorder for use in the treatment or prevention of muscle disorder in a subject having an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule. Any of the muscle disorder therapeutic agents that treat, prevent, or inhibit muscle disorder described herein can be used herein. Any of the FNIP1 variant nucleic acid molecules and/or FLCN variant nucleic acid molecules disclosed herein can be used herein. In some embodiments, the FNIP1 variant nucleic acid molecule and/or the FLCN variant nucleic acid molecule is an FNIP1 variant genomic nucleic acid molecule or FLCN variant genomic nucleic acid molecule that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule.

The present disclosure also provides uses of muscle disorder therapeutic agents that treat, prevent, or inhibit muscle disorder for use in the preparation of a medicament for treating or preventing muscle disorder in a subject having an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule. Any of the muscle disorder therapeutic agents that treat, prevent, or inhibit muscle disorder described herein can be used herein. Any of the FNIP1 variant nucleic acid molecules and/or FLCN variant nucleic acid molecules disclosed herein can be used herein. In some embodiments, the FNIP1 variant nucleic acid molecule and/or the FLCN variant nucleic acid molecule is an FNIP1 variant genomic nucleic acid molecule or FLCN variant genomic nucleic acid molecule that comprises any one or more of

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the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule.

The present disclosure also provides FNIP1 inhibitors for use in the treatment or prevention of muscle disorder in a subject that is FNIP1 reference or is heterozygous for an FNIP1 variant nucleic acid molecule. Any of the FNIP1 inhibitors described herein can be used herein. Any of the FNIP1 variant nucleic acid molecules disclosed herein can be used herein. In some embodiments, the FNIP1 variant nucleic acid molecule and/or the FLCN variant nucleic acid molecule is an FNIP1 variant genomic nucleic acid molecule or FLCN variant genomic nucleic acid molecule that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule.

The present disclosure also provides FNIP1 inhibitors in the preparation of a medicament for treating or preventing muscle disorder in a subject that is FNIP1 reference or is heterozygous for an FNIP1 variant nucleic acid molecule. Any of the FNIP1 inhibitors described herein can be used herein. Any of the FNIP1 variant nucleic acid molecules disclosed herein can be used herein. In some embodiments, the FNIP1 variant nucleic acid molecule and/or the FLCN variant nucleic acid molecule is an FNIP1 variant genomic nucleic acid molecule or FLCN variant genomic nucleic acid molecule that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule.

The present disclosure also provides FLCN inhibitors for use in the treatment or prevention of muscle disorder in a subject that is FLCN reference or is heterozygous for an FLCN variant nucleic acid molecule. Any of the FLCN inhibitors described herein can be used herein. Any of the FLCN variant nucleic acid molecules disclosed herein can be used herein. In some embodiments, the FLCN variant nucleic acid molecule is an FLCN variant genomic nucleic acid molecule that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule.

The present disclosure also provides FLCN inhibitors in the preparation of a medicament for treating or preventing muscle disorder in a subject that is FLCN reference or is heterozygous for an FLCN variant nucleic acid molecule. Any of the FLCN inhibitors described herein can be used herein. Any of the FLCN variant nucleic acid molecules disclosed herein can

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be used herein. In some embodiments, the FLCN variant nucleic acid molecule is a FLCN variant genomic nucleic acid molecule that comprises any one or more of the genetic variations described herein, or is an mRNA molecule produced therefrom, or is a cDNA molecule produced from the mRNA molecule.

5 In some embodiments, the FNIP1 inhibitor and/or the FLCN inhibitor, and the muscle disorder therapeutic agent are disposed within a pharmaceutical composition. In some embodiments, the FNIP1 inhibitor and/or the FLCN inhibitor are disposed within a first pharmaceutical composition and the muscle disorder therapeutic agent is disposed within a second pharmaceutical composition. In some embodiments, the first pharmaceutical
10 composition and the second pharmaceutical composition are administered simultaneously. In some embodiments, the first pharmaceutical composition is administered before the second pharmaceutical composition. In some embodiments, the first pharmaceutical composition is administered after the second pharmaceutical composition.

 All patent documents, websites, other publications, accession numbers and the like
15 cited above or below are incorporated by reference in their entirety for all purposes to the same extent as if each individual item were specifically and individually indicated to be so incorporated by reference. If different versions of a sequence are associated with an accession number at different times, the version associated with the accession number at the effective filing date of this application is meant. The effective filing date means the earlier of the actual
20 filing date or filing date of a priority application referring to the accession number if applicable. Likewise, if different versions of a publication, website or the like are published at different times, the version most recently published at the effective filing date of the application is meant unless otherwise indicated. Any feature, step, element, embodiment, or aspect of the present disclosure can be used in combination with any other feature, step, element,
25 embodiment, or aspect unless specifically indicated otherwise. Although the present disclosure has been described in some detail by way of illustration and example for purposes of clarity and understanding, it will be apparent that certain changes and modifications may be practiced within the scope of the appended claims.

 The following examples are provided to describe the embodiments in greater detail.
30 They are intended to illustrate, not to limit, the claimed embodiments. The following examples provide those of ordinary skill in the art with a disclosure and description of how the compounds, compositions, articles, devices and/or methods described herein are made and

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evaluated and are intended to be purely exemplary and are not intended to limit the scope of any claims. Efforts have been made to ensure accuracy with respect to numbers (such as, for example, amounts, temperature, etc.), but some errors and deviations may be accounted for. Unless indicated otherwise, parts are parts by weight, temperature is in °C or is at ambient
5 temperature, and pressure is at or near atmospheric.

Examples

Example 1: General Methods

Participating cohorts

10 Genetic association studies were performed in individuals of African or Admixed African, Admixed American, European, and East and South Asian ancestry from the United Kingdom Biobank (UKB) cohort (Bycroft et al., Nature, 2018, 562, 203-09; and Van Hout et al., Nature, 2020, 586, 749-56), the MyCode Community Health Initiative cohort from the Geisinger Health System (GHS) (Carey et al., Genet. Med., 2016, 18, 906-13), the University of
15 Pennsylvania Medicine BioBank (UPENN-PMBB), the Malmö Diet and Cancer Study (MDCS) (Berglund et al., J. Int. Med., 1993, 233, 45-51), the Mount Sinai's BioMe Personalized Medicine Cohort (SINAI) (Gottesman et al., Genet. Med., 2013, 15, 761-71), the Indiana Biobank (INDIANA), the Colorado Biobanked and Prospective Collection Project (COLORADO), the UCLA Biobank (UCLA), the Mayo Clinic Biobank (MAYO-CLINIC), the University of Pennsylvania Highly
20 Consanguineous Cohort of Pakistani individuals enrolled in the Center for Non-Communicable Diseases (CNCD), the National Institute of Diabetes and Digestive and Kidney Diseases Sequencing in Pima Indians (NIDDK) (Knowler et al., Am. J. Epidemiol., 1978, 108, 497-505), the Mexico City Prospective Study (MCPS) (Tapia-Conyer et al., Int. J. Epidemiol., 2006, 35, 243-9) and the University of Texas Southwestern Dallas Heart Expansion Study - Dallas Biobank (UTSW-
25 COHEN).

The UKB is a population-based cohort study of people aged between 40 and 69 years recruited through 22 testing centers in the UK between 2006-2010. Exome sequencing and phenotype data were available up to 432,015 individuals. The GHS MyCode study is a health system-based cohort of patients from Central and Eastern Pennsylvania (USA) recruited in
30 2007-2019. A total of 134,731 participants from GHS with available whole-exome sequencing and phenotype data were included. SINAI is an electronic health record-linked clinical care cohort, of which 21,673 individuals had available phenotypes and exome sequencing data. The

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MDCS is a population-based prospective cohort that included 5,215 individuals with available phenotype and exome sequencing data. The UPENN-PMBB included a total of 26,022 individuals with available phenotype and exome sequencing data. The INDIANA biobank included 5,389 participants with exome sequencing and phenotypic data. The MCPS is a population-based prospective study that included 33,935 individuals with phenotype and exome sequencing data. The CNCD is a population-based study of Pakistani individuals and included 34,831 individuals with phenotype and exome sequencing data. The NIDDK included 5,175 with both phenotype and exome sequencing data. The COLORADO, UCLA and MAYO-CLINIC are hospital-based electronic health record data that provided genotypic and phenotypic data on 35,320, 27,932 and 81,132. The UTSW-COHEN is a population-based cohort of African- and Hispanic- Americans in the city of Dallas that included 13,888 individuals.

Phenotype definitions

Blood lipid levels were measured from samples drawn during the first visit to study center for population-based studies like UKB and MDCS, while they were obtained as the median measurement from cohorts using electronic healthcare record data. In general, LDL cholesterol levels were estimated using the Friedewald equation for the except for the UKB where direct LDL measurements were available. Individuals known to be on lipid lowering medication had their pre-treatment lipid levels estimated using a correction factor.

Liver MRI Phenotypes

A subset of participants in UKB underwent magnetic resonance imaging (MRI) of the liver (Littlejohns et al., Nat. Commun., 2020, 11, 2624). For liver fat imaging acquisition, approximately 10,000 subjects were imaged under a Dixon gradient echo protocol, while the remaining set of individuals, who underwent imaging from 2016 onwards, were imaged using an IDEAL sequence (Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation) protocol. Data from this acquisition are provided as a series of complex-valued 2D images per subject. The in-plane pixel size is 2.5x2.5 mm; slice thickness is 6 mm. All images were acquired on Siemens MAGNETOM clinical MRI scanners.

Measurements of liver fat percentage (proton density liver fat fraction; PDFF), a measure of the proportion of fat content in the liver, were obtained by applying pre-defined mathematical models after segmenting the liver on liver MRI images (Hernando et al., Magn. Reason. Med., 2012, 67, 638-44). The implementation was validated using a publicly available phantom dataset containing vials of varying concentrations of fat (Hernando et al., Magn.

Reason. Med., 2017, 77, 1516-24). PDFF was estimated as the fraction of fat signal relative to total fat plus water signal. Pixels belonging to the liver were segmented using a Li thresholding approach for PDFF maps to identify liver tissue. To obtain a summary measure of each trait per subject, all pixels within the liver were averaged for each parametric map. PDFF was then used
5 as the outcome for the analysis. Further details on the derivation of these phenotypes have been published (O'Dushlaine et al., Genome-wide association study of liver fat, iron, and extracellular fluid fraction in the UK Biobank', medRxiv: 2021.10.25.21265127).

Phenotype definitions

Clinical laboratory measurements for ALT, total cholesterol, LDL cholesterol, HDL
10 cholesterol and triglycerides were extracted from electronic health records (EHRs) for participants from the GHS, UPENN-PMBB, SINAI, INDIANA, UCLA, COLORADO, and MAYO-CLINIC biobanks or measured at recruitment for UKB, MDCS, CNCD, NIDDK, UTSW-COHEN. GHS, UPENN-PMBB, SINAI, INDIANA, UCLA, COLORADO, and MAYO-CLINIC, median values were calculated for all participants with two or more measurements. In UKB, ALT, AST, total
15 cholesterol, LDL cholesterol, HDL cholesterol and triglycerides were measured by IFCC (International Federation of Clinical Chemistry) analysis on a Beckman Coulter AU5800 at the baseline visit of the study and averaged in case of multiple measurements. Prior to genetic association analysis, continuous phenotype values were transformed by the inverse standard normal function, applied within each ancestry group and separately in men and women.

20 Disease outcomes were defined according to the International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and ICD-10) and Read codes stored in EHRs, and self-reports were used when available; all of which and combined into single variables to classify individuals into cases or controls. Individuals with type 2 diabetes were identified using a previously described algorithm (Eastwood et al., PLoS One, 2016, 11, e0162388). Individuals
25 with coronary artery disease or liver diseases were identified as described in Table 6, combining EHR records, self-reports and ALT measurements.

Individuals with or without disease were identified using EHR records and self-reports. OPCS4 codes (operation procedures), f.20002 (self-reported disease) and f.20004 (self-reported operation procedures) variables were specific to UKB. In each cohort, EHR records with ICD-9 or
30 read codes were translated to ICD-10 codes.

Table 2

Disease	Case definition	Control exclusion
Non-alcoholic liver disease	ICD10: K721,K740,K741,K742,K746, K758,K760	ICD10: K70,K71,K72,K73,K74,K75,K76,K77,I81, I85,I982,I983,I864,T864,Z944,C220 OPCS4: G10, G144,J01 f.20002: 1604,1158,1141 ALT: >33 IU/L for men and >24 IU/L for women

Type 2 diabetes cases were adjudicated in each cohort on the basis of one or more of the following criteria: 1) an electronic health record of type 2 diabetes (using International Classification of Diseases, Tenth Revision (ICD-10) diagnosis codes E11 or O24.1 or
5 corresponding Ninth Revision (ICD-9) codes), in at least one inpatient encounter or at least two outpatient encounters or if noted as a cause of death; 2) a glycemic biomarker value (HbA1c, random or fasting glucose) in the diabetic range (Diabetes Care, 2021, 44(Suppl 1), S15-S33); 3) a prescription record of anti-diabetic medication use; 4) a self-reported physician diagnosis of type 2 diabetes; 5) entry on a diabetes registry as a type 2 diabetes case. Where possible,
10 individuals were excluded from the case pool if they had a potential diagnosis of type 1 diabetes mellitus (using ICD-10 codes E10 or O24.0, and a prescription record that included insulin only in the absence of other diabetic medication). Individuals not meeting any of the criteria for diabetes case status were used as controls. In addition, individuals were excluded
15 from the control group if they met any of the following criteria: 1) an electronic health record diagnosis pertaining to any potential type of diabetes mellitus or a family history of diabetes; 2) a glycemic biomarker value in the prediabetic range; 3) any other cohort-specific phenotype that potentially indicated a diagnosis of diabetes mellitus (e.g., a disease registry entry or self-reported diagnosis of non-specific diabetes).

Genotype data

20 High coverage whole exome sequencing was performed as previously described (Science, 2016, 354:aaf6814; and Nature, 2020, 586, 749-756) and as summarized below.

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NimbleGen probes (VCRome; for part of the GHS cohort) or a modified version of the xGen design available from Integrated DNA Technologies (IDT; for the rest of GHS and other cohorts) were used for target sequence capture of the exome. A unique 6 base pair (bp) barcode (VCRome) or 10 bp barcode (IDT) was added to each DNA fragment during library preparation

5 to facilitate multiplexed exome capture and sequencing. Equal amounts of sample were pooled prior to exome capture. Sequencing was performed using 75 bp paired-end reads on Illumina v4 HiSeq 2500 (for part of the GHS cohort) or NovaSeq (for the rest of GHS and other cohorts) instruments. Sequencing had a coverage depth (i.e., number of sequence-reads covering each nucleotide in the target areas of the genome) sufficient to provide greater than 20x coverage

10 over 85% of targeted bases in 96% of VCRome samples and 20x coverage over 90% of targeted bases in 99% of IDT samples. Data processing steps included sample de-multiplexing using Illumina software, alignment to the GRCh38 Human Genome reference sequence including generation of binary alignment and mapping files (BAM), processing of BAM files (e.g., marking of duplicate reads and other read mapping evaluations). Variant calling was performed using

15 the GLNexus system. Variant mapping and annotation were based on the GRCh38 Human Genome reference sequence and Ensembl v85 gene definitions using the snpEff software. The snpEff predictions that involve protein-coding transcripts with an annotated start and stop were then combined into a single functional impact prediction by selecting the most deleterious functional effect class for each gene. The hierarchy (from most to least deleterious)

20 for these annotations was frameshift, stop-gain, stop-loss, splice acceptor, splice donor, stop-lost, in-frame indel, missense, other annotations. Predicted LOF genetic variants included: a) insertions or deletions resulting in a frameshift, b) insertions, deletions or single nucleotide variants resulting in the introduction of a premature stop codon or in the loss of the transcription start site or stop site, and c) variants in donor or acceptor splice sites. Missense

25 variants were classified for likely functional impact according to the number of *in silico* prediction algorithms that predicted deleteriousness using SIFT (Adzhubei et al., Nat. Methods, 2010, 7, 248-9) and Polyphen2_HVAR (Adzhubei et al., Nat. Methods, 2010, 7, 248-9), LRT (Chun et al., Genome Res., 2009, 19, 1553-61) and MutationTaster (Schwarz et al., Nat. Methods, 2010, 7, 575-6). For each gene, the alternative allele frequency (AAF) and functional

30 annotation of each variant determined inclusion into these 7 gene burden exposures: 1) pLOF variants with AAF < 1%; 2) pLOF or missense variants predicted deleterious by 5/5 algorithms with AAF < 1%; 3) pLOF or missense variants predicted deleterious by 5/5 algorithms with AAF <

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0.1%; 4) pLOF or missense variants predicted deleterious by at least 1/5 algorithms with AAF < 1%; 5) pLOF or missense variants predicted deleterious by at least 1/5 algorithms with AAF < 0.1%; 6) pLOF or any missense with AAF < 1%; 7) pLOF or any missense variants with AAF < 0.1%.

5 *Association analysis of gene burden of rare loss of function variation*

Association between the burden of rare predicted loss-of-function or missense variants in a given gene and phenotype was examined by fitting a linear (for quantitative traits) or first bias-corrected logistic (for binary traits) regression model adjusted for a polygenic score that approximates a genomic kinship matrix using REGENIE v1.0. Analyses were stratified by ancestry and adjusted for age, age², sex, age-by-sex and age²-by-sex interaction terms, experimental batch-related covariates, 10 common variant-derived principal components, and 20 rare variant-derived principal components. Results across cohorts for each variant-phenotype association were combined using fixed effects inverse variance weighted meta-analysis. In gene burden tests, all individuals were labeled as heterozygotes if they carried one or more qualifying rare variant (as described above based on frequency and functional annotation) and as homozygotes if they carried any qualifying variant in the homozygous state. This “composite genotype” was then used to test for association.

20 **Example 2: Loss of Function of the Genes Encoding FNIP1 and FLCN is Associated with Lower Levels of Triglycerides, Alanine Aminotransferase, Liver Fat by MRI, HbA1c and Waist-to-Hip Ratio and Protection from Type 2 Diabetes**

Exome sequencing data was analyzed for participants from the Geisinger Health System MyCode Community Health Initiative study (GHS), Malmö Diet and Cancer Study (MDCS), Mount Sinai’s BioMe personalized medicine cohort (SINAI), the UK Biobank (UKB), the University of Pennsylvania Penn Medicine Biobank (UPENN-PMBB), the Indiana University Biobank (INDIANA), the Colorado Biobanked and Prospective Collection Project (COLORADO), the UCLA Biobank (UCLA), the Mayo Clinic Biobank (MAYO-CLINIC), the University of Pennsylvania Highly Consanguineous Cohort (CNCD), the National Institute of Diabetes and Digestive and Kidney Diseases Sequencing in Pima Indians (NIDDK), the Mexico City Prospective Study (MCPS) and the University of Texas Southwestern Dallas Heart Expansion Study - Dallas Biobank (UTSW-COHEN). In a large exome-wide association analyses of rare coding variation

with blood lipids, FNIP1 and FLCN loss-of-function variants were identified to be associated with a decrease in triglyceride, LDL cholesterol, and alanine aminotransferase levels (ALT).

Compared to non-carriers, carriers of rare predicted loss-of-function variants in FNIP1 and FLCN had lower levels triglycerides (-35 mg/dL and -21 mg/dL, respectively), LDL
5 cholesterol (-7 mg/dL and -4 mg/dL, respectively) and apolipoprotein B (-7 mg/dL and -5 mg/dL, respectively (see, Table 3). Carriers of loss-of-function variants in both genes had lower levels of alanine aminotransferase, and those with FLCN loss-of-function variants had significantly lower liver fat and inflammation levels as measured by MRI (see, Table 4). FNIP1 rare predicted loss-
of-function and deleterious missense were associated with lower odds of non-alcoholic liver
10 disease (see, Table 5). Carriers of loss-of-function or deleterious missense variants in both genes had favorable fat distribution as indicated by lower waist-to-hip ratio, lower body fat percentage, lower HbA1c and lower odds of type 2 diabetes (see, Table 6 and Table 7).

Table 3: Rare predicted loss of function variants in FNIP1 and FLCN are associated with lower levels of LDL cholesterol, triglycerides, and apolipoprotein levels

Trait	Gene pLoF	Allele frequency of carriers	Genotype count (RR RA AA)	Effect size (95% confidence interval) (SD units / Clinical units)	P-value
Triglyceride / HDL Ratio	FNIP1	8x10 ⁻⁵	771,868 / 116 / 2	-0.44 (-0.60, -0.27) SD / -2.03 (-2.79, -1.27) ratio	2x10 ⁻⁷
	FLCN	2x10 ⁻⁴	795,771 / 286 / 0	-0.21 (-0.32, -0.11) SD / -0.99 (-1.49, -0.49) ratio	0.0001
Triglycerides	FNIP1	8x10 ⁻⁵	820,763 / 121 / 2	-0.38 (-0.54, -0.22) SD / -34.78 (-49.47, -20.09) mg/dL	3x10 ⁻⁶
	FLCN	2x10 ⁻⁴	835,898 / 298 / 0	-0.23 (-0.33, -0.12) SD / -20.93 (-30.61, -11.24) mg/dL	2x10 ⁻⁵

HDL cholesterol	FNIP1	8x10 ⁻⁵	778,162 / 119 / 2	0.41 (0.25, 0.57) SD / 6.33 (3.88, 8.77) mg/dL	4x10 ⁻⁷
	FLCN	2x10 ⁻⁴	800,789 / 289 / 0	0.09 (-0.01, 0.20) SD / 1.42 (-0.20, 3.04) mg/dL	0.09
LDL cholesterol	FNIP1	8x10 ⁻⁵	814,013 / 120 / 2	-0.19 (-0.35, -0.03) SD / -7.03 (-12.84, -1.23) mg/dL	0.02
	FLCN	2x10 ⁻⁴	828,975 / 297 / 0	-0.12 (-0.22, -0.01) SD / -4.33 (-8.15, -0.51) mg/dL	0.03
Non-HDL cholesterol	FNIP1	8x10 ⁻⁵	703,131 / 107 / 2	-0.26 (-0.43, -0.10) SD / -10.75 (-17.51, -4.00) mg/dL	0.002
	FLCN	2x10 ⁻⁴	726,992 / 252 / 0	-0.20 (-0.31, -0.09) SD / -8.05 (-12.63, -3.47) mg/dL	0.0006
Apolipoprotein B	FNIP1	7x10 ⁻⁵	489,524 / 72 / 0	-0.30 (-0.50, -0.10) SD / -7.25 (-12.15, -2.34) mg/dL	0.004
	FLCN	2x10 ⁻⁴	490,948 / 156 / 0	-0.19 (-0.33, -0.06) SD / -4.74 (-8.07, -1.42) mg/dL	0.005

Effect sizes are given in standard deviation (SD) and clinical units. RR: count of homozygous individuals for the reference allele, RA: count of heterozygous individuals carrying one pLOF variant, AA: count of homozygous individuals carrying pLOF variants in both alleles.

5 Table 4: Rare predicted loss of function variants in *FNIP1* and *FLCN* are associated with lower levels of liver enzymes and liver fat and inflammation as measured by MRI

Trait	Gene pLoF	Allele frequency	Genotype count (RR RA AA)	Effect size (95% confidence interval)	P-value
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		of carriers		(SD units / Clinical units)	
ALT	FNIP1	7×10^{-5}	773,854 / 107 / 2	-0.35 (-0.53, -0.18) SD / -7.07 (-10.56, -3.59) U/L	7×10^{-5}
	FLCN	2×10^{-4}	785,764 / 274 / 0	-0.13 (-0.24, -0.02) SD / -2.63 (-4.89, -0.37) U/L	0.02
AST	FNIP1	7×10^{-5}	789,168 / 111 / 2	-0.27 (-0.44, -0.10) SD / -4.22 (-6.87, -1.57) U/L	0.002
	FLCN	2×10^{-4}	799,881 / 276 / 0	-0.06 (-0.17, 0.06) SD / -0.87 (-2.62, 0.87) U/L	0.33
Liver Fat % by MRI	FNIP1	8×10^{-5}	37,039 / 6 / 0	-0.42 (-1.16, 0.33) SD / -2.05 (-5.71, 1.62) %	0.27
	FLCN	2×10^{-4}	36,749 / 11 / 0	-0.72 (-1.30, -0.15) SD / -3.55 (-6.38, -0.72) %	0.01
Liver Inflamm ation by MRI	FNIP1	8×10^{-5}	37,039 / 6 / 0	-0.25 (-0.98, 0.48) SD / -11.37 (-44.46, 21.72)	0.5
	FLCN	4×10^{-4}	36,734 / 26 / 0	-0.43 (-0.80, -0.06) SD / -19.64 (-36.57, -2.71)	0.02

Effect sizes are given in standard deviation (SD) and clinical units. RR: count of homozygous individuals for the reference allele, RA: count of heterozygous individuals carrying one pLOF variant, AA: count of homozygous individuals carrying pLOF variants in both alleles.

5 Table 5: Rare predicted loss of function and deleterious missense variants in *FNIP1* are associated with odds of non-alcoholic liver disease

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Gene Variation	Allele frequency of carriers	Genotype count cases (RR RA AA)	Genotype count controls (RR RA AA)	Odds Ratio (95% CI)	P value
FLCN pLOF	2×10^{-4}	33,886/13/0	636,050/236/0	1.06 (0.61, 1.86)	0.84
FLCN pLOF plus deleterious missense	3×10^{-3}	37,159/172/0	669,457/3,840/1	0.97 (0.82, 1.13)	0.67
FNIP1 pLOF	9×10^{-5}	27,265/2/1	564,649/96/1	1.17 (0.52, 2.66)	0.7
FNIP1 pLOF plus deleterious missense	1×10^{-2}	37,286/906/3	660,137/17,473/39	0.90 (0.83, 0.96)	0.002

RR: count of homozygous individuals for the reference allele, RA: count of heterozygous individuals carrying one pLOF or pLOF+deleterious missense variant, AA: count of homozygous individuals carrying pLOF+deleterious missense variants in both alleles.

- 5 Table 6: Rare predicted loss of function variants in FNIP1 and FLCN are associated with lower waist to hip ratio, body fat percentage and HbA1c levels

Trait	Gene pLoF	Allele frequency of carriers	Genotype count (RR RA AA)	Effect size (95% confidence interval) (SD units / Clinical units)	P-value
Waist Hip Ratio adjusted for BMI	FNIP1	8×10^{-5}	670,295/105/0	-0.24 (-0.42, -0.06) SD / -0.02 (-0.03, -0.00) ratio	0.008
	FLCN	2×10^{-4}	671,779/217/0	-0.11 (-0.23, 0.02) SD / -0.01 (-0.02, 0.00) ratio	0.09
	FNIP1	7×10^{-5}	484,446/66/0	-0.31 (-0.53, -0.08) SD /	0.007

(BIA) Body fat %				-2.62 (-4.53, -0.71) %	
	FLCN	2x10 ⁻⁴	485,932/157/0	-0.18 (-0.32, -0.03) SD / -1.50 (-2.74, -0.27) %	0.02
HbA1c	FNIP1	8x10 ⁻⁵	840,079/124/2	-0.21 (-0.36, -0.06) SD / -0.22 (-0.37, -0.06) %	0.006
	FLCN	2x10 ⁻⁴	844,518/275/0	-0.14 (-0.25, -0.04) SD / -0.15 (-0.26, -0.04) %	0.007

Effect sizes are given in standard deviation (SD) and clinical units. RR: count of homozygous individuals for the reference allele, RA: count of heterozygous individuals carrying one pLOF variant, AA: count of homozygous individuals carrying pLOF variants in both alleles.

5 Table 7: Rare predicted loss of function and deleterious missense variants in *FNIP1* and *FLCN* are associated with lower odds of type 2 diabetes

Gene Variation	Allele frequency of carriers	Genotype count cases (RR RA AA)	Genotype count controls (RR RA AA)	Odds Ratio (95% CI)	P value
<i>FLCN</i> pLOF	2x10 ⁻⁴	140,532/38/0	644,837/249/0	0.68 (0.48,0.97)	0.03
<i>FLCN</i> pLOF plus deleterious missense	3x10 ⁻³	153,579/729/2	689,124/4,105/1	0.86 (0.79,0.94)	0.0006
<i>FNIP1</i> pLOF	8x10 ⁻⁵	115,620/17/0	563,973/88/0	0.78 (0.47,1.32)	0.36
<i>FNIP1</i> pLOF plus deleterious missense	1x10 ⁻²	153,603/4,025/15	684,824/16,901/36	0.95 (0.92,0.99)	0.02

RR: count of homozygous individuals for the reference allele, RA: count of heterozygous individuals carrying one pLOF or pLOF+deleterious missense variant, AA: count of homozygous individuals carrying pLOF+deleterious missense variants in both alleles.

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Table 8: Predicted loss of function or deleterious missense variants in FNIP1 identified by whole exome sequencing

Variant	Effect	hgvs	hgvs
5:131644687:A:G	stop_lost	ENST00000510461.6:c.3499T>C	ENSP00000421985.1:p.Ter116 7Gln>Ter3
5:131644689:A:T	missense	ENST00000510461.6:c.3497T>A	ENSP00000421985.1:p.Leu116 6His
5:131644701:G:A	missense	ENST00000510461.6:c.3485C>T	ENSP00000421985.1:p.Alala116 2Val
5:131644702:C:T	missense	ENST00000510461.6:c.3484G>A	ENSP00000421985.1:p.Alala116 2Thr
5:131644707:T:C	missense	ENST00000510461.6:c.3479A>G	ENSP00000421985.1:p.Tyr116 0Cys
5:131644707:T:G	missense	ENST00000510461.6:c.3479A>C	ENSP00000421985.1:p.Tyr116 0Ser
5:131644708:A:C	missense	ENST00000510461.6:c.3478T>G	ENSP00000421985.1:p.Tyr116 0Asp
5:131644717:G:A	missense	ENST00000510461.6:c.3469C>T	ENSP00000421985.1:p.His115 7Tyr
5:131644717:G:T	missense	ENST00000510461.6:c.3469C>A	ENSP00000421985.1:p.His115 7Asn
5:131644720:T:C	missense	ENST00000510461.6:c.3466A>G	ENSP00000421985.1:p.Thr115 6Ala
5:131644721:G:C	missense	ENST00000510461.6:c.3465C>G	ENSP00000421985.1:p.Ser115 5Arg
5:131644725:G:A	missense	ENST00000510461.6:c.3461C>T	ENSP00000421985.1:p.Alala115 4Val
5:131644726:C:T	missense	ENST00000510461.6:c.3460G>A	ENSP00000421985.1:p.Alala115 4Thr
5:131644728:A:G	missense	ENST00000510461.6:c.3458T>C	ENSP00000421985.1:p.Val115 3Ala
5:131644734:G:A	missense	ENST00000510461.6:c.3452C>T	ENSP00000421985.1:p.Alala115 1Val

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5:131644735:C:A	missense	ENST00000510461.6:c.3451G>T	ENSP00000421985.1:p.Ala115 1Ser
5:131644735:C:T	missense	ENST00000510461.6:c.3451G>A	ENSP00000421985.1:p.Ala115 1Thr
5:131644738:G:C	missense	ENST00000510461.6:c.3448C>G	ENSP00000421985.1:p.Leu115 0Val
5:131644744:G:A	missense	ENST00000510461.6:c.3442C>T	ENSP00000421985.1:p.Pro114 8Ser
5:131644759:C:T	missense	ENST00000510461.6:c.3427G>A	ENSP00000421985.1:p.Glu114 3Lys
5:131644761:A:G	missense	ENST00000510461.6:c.3425T>C	ENSP00000421985.1:p.Ile1142 Thr
5:131647089:C:T	splice_do nor	ENST00000510461.6:c.3422+1G >A	NA
5:131647090:C:A	missense	ENST00000510461.6:c.3422G>T	ENSP00000421985.1:p.Gly114 1Val
5:131647090:C:T	missense	ENST00000510461.6:c.3422G>A	ENSP00000421985.1:p.Gly114 1Glu
5:131647091:C:A	missense	ENST00000510461.6:c.3421G>T	ENSP00000421985.1:p.Gly114 1Trp
5:131647093:A:G	missense	ENST00000510461.6:c.3419T>C	ENSP00000421985.1:p.Leu114 0Pro
5:131647093:A:T	missense	ENST00000510461.6:c.3419T>A	ENSP00000421985.1:p.Leu114 0Gln
5:131647100:C:A	missense	ENST00000510461.6:c.3412G>T	ENSP00000421985.1:p.Val113 8Leu
5:131647106:G:C	missense	ENST00000510461.6:c.3406C>G	ENSP00000421985.1:p.Leu113 6Val
5:131647107:C:A	missense	ENST00000510461.6:c.3405G>T	ENSP00000421985.1:p.Glu113 5Asp
5:131647111:T:C	missense	ENST00000510461.6:c.3401A>G	ENSP00000421985.1:p.Lys113 4Arg
5:131647112:T:C	missense	ENST00000510461.6:c.3400A>G	ENSP00000421985.1:p.Lys113 4Glu

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5:131647117:T:G	missense	ENST00000510461.6:c.3395A>C	ENSP00000421985.1:p.His113 2Pro
5:131647118:G:A	missense	ENST00000510461.6:c.3394C>T	ENSP00000421985.1:p.His113 2Tyr
5:131647123:C:C G	frameshift	ENST00000510461.6:c.3388dup	ENSP00000421985.1:p.Arg113 0ProfsTer14
5:131647123:C:G	missense	ENST00000510461.6:c.3389G>C	ENSP00000421985.1:p.Arg113 0Pro
5:131647123:C:T	missense	ENST00000510461.6:c.3389G>A	ENSP00000421985.1:p.Arg113 0His
5:131647124:G:A	missense	ENST00000510461.6:c.3388C>T	ENSP00000421985.1:p.Arg113 0Cys
5:131647124:G:C	missense	ENST00000510461.6:c.3388C>G	ENSP00000421985.1:p.Arg113 0Gly
5:131647125:C:T	missense	ENST00000510461.6:c.3387G>A	ENSP00000421985.1:p.Met11 29Ile
5:131647129:T:C	missense	ENST00000510461.6:c.3383A>G	ENSP00000421985.1:p.Gln112 8Arg
5:131647132:C:G	missense	ENST00000510461.6:c.3380G>C	ENSP00000421985.1:p.Gly112 7Ala
5:131647135:C:G	missense	ENST00000510461.6:c.3377G>C	ENSP00000421985.1:p.Arg112 6Thr
5:131647145:C:T	missense	ENST00000510461.6:c.3367G>A	ENSP00000421985.1:p.Glu112 3Lys
5:131647151:G:C	missense	ENST00000510461.6:c.3361C>G	ENSP00000421985.1:p.Leu112 1Val
5:131647154:T:G	missense	ENST00000510461.6:c.3358A>C	ENSP00000421985.1:p.Met11 20Leu
5:131647162:T:C	missense	ENST00000510461.6:c.3350A>G	ENSP00000421985.1:p.Lys111 7Arg
5:131647165:A:T	missense	ENST00000510461.6:c.3347T>A	ENSP00000421985.1:p.Phe11 16Tyr
5:131647166:A:G	missense	ENST00000510461.6:c.3346T>C	ENSP00000421985.1:p.Phe11 16Leu

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5:131647174:T:C	missense	ENST00000510461.6:c.3338A>G	ENSP00000421985.1:p.Glu111 3Gly
5:131647175:C:T	missense	ENST00000510461.6:c.3337G>A	ENSP00000421985.1:p.Glu111 3Lys
5:131647183:C:A	missense	ENST00000510461.6:c.3329G>T	ENSP00000421985.1:p.Arg111 0Leu
5:131647183:C:T	missense	ENST00000510461.6:c.3329G>A	ENSP00000421985.1:p.Arg111 0Gln
5:131647184:G:A	missense	ENST00000510461.6:c.3328C>T	ENSP00000421985.1:p.Arg111 0Trp
5:131647187:C:G	missense	ENST00000510461.6:c.3325G>C	ENSP00000421985.1:p.Asp110 9His
5:131647188:T:G	missense	ENST00000510461.6:c.3324A>C	ENSP00000421985.1:p.Glu110 8Asp
5:131647190:C:T	missense	ENST00000510461.6:c.3322G>A	ENSP00000421985.1:p.Glu110 8Lys
5:131647195:T:C	missense	ENST00000510461.6:c.3317A>G	ENSP00000421985.1:p.His110 6Arg
5:131647195:T:G	missense	ENST00000510461.6:c.3317A>C	ENSP00000421985.1:p.His110 6Pro
5:131647196:G:G CATT	frameshift	ENST00000510461.6:c.3312_33 15dup	ENSP00000421985.1:p.His110 6AsnfsTer4
5:131647199:T:A	missense	ENST00000510461.6:c.3313A>T	ENSP00000421985.1:p.Met11 05Leu
5:131647199:T:C	missense	ENST00000510461.6:c.3313A>G	ENSP00000421985.1:p.Met11 05Val
5:131647202:C:T	missense	ENST00000510461.6:c.3310G>A	ENSP00000421985.1:p.Val110 4Ile
5:131647206:C:C TG	splice_acceptor	ENST00000510461.6:c.3307- 3_3307-2dup	NA
5:131651807:T:C	missense	ENST00000510461.6:c.3301A>G	ENSP00000421985.1:p.Asn110 1Asp
5:131651810:G:A	missense	ENST00000510461.6:c.3298C>T	ENSP00000421985.1:p.Pro110 0Ser

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5:131651810:G:T	missense	ENST00000510461.6:c.3298C>A	ENSP00000421985.1:p.Pro110 0Thr
5:131651814:C:G	missense	ENST00000510461.6:c.3294G>C	ENSP00000421985.1:p.Leu109 8Phe
5:131651814:CA: C	frameshif t	ENST00000510461.6:c.3293del	ENSP00000421985.1:p.Leu109 8CysfsTer7
5:131651817:GT: G	frameshif t	ENST00000510461.6:c.3290del	ENSP00000421985.1:p.Asn109 7ThrfsTer8
5:131651818:T:A	missense	ENST00000510461.6:c.3290A>T	ENSP00000421985.1:p.Asn109 7Ile
5:131651819:T:G	missense	ENST00000510461.6:c.3289A>C	ENSP00000421985.1:p.Asn109 7His
5:131651821:T:C	missense	ENST00000510461.6:c.3287A>G	ENSP00000421985.1:p.His109 6Arg
5:131651824:T:A	missense	ENST00000510461.6:c.3284A>T	ENSP00000421985.1:p.Lys109 5Met
5:131651824:T:C	missense	ENST00000510461.6:c.3284A>G	ENSP00000421985.1:p.Lys109 5Arg
5:131651825:T:C	missense	ENST00000510461.6:c.3283A>G	ENSP00000421985.1:p.Lys109 5Glu
5:131651828:A:G	missense	ENST00000510461.6:c.3280T>C	ENSP00000421985.1:p.Tyr109 4His
5:131651831:G:C	missense	ENST00000510461.6:c.3277C>G	ENSP00000421985.1:p.Leu109 3Val
5:131651834:G:T	missense	ENST00000510461.6:c.3274C>A	ENSP00000421985.1:p.Gln109 2Lys
5:131651834:GA A:G	frameshif t	ENST00000510461.6:c.3272_32 73del	ENSP00000421985.1:p.Leu109 1ProfsTer4
5:131651837:G:C	missense	ENST00000510461.6:c.3271C>G	ENSP00000421985.1:p.Leu109 1Val
5:131651839:G:A	missense	ENST00000510461.6:c.3269C>T	ENSP00000421985.1:p.Thr109 0Ile
5:131651840:T:C	missense	ENST00000510461.6:c.3268A>G	ENSP00000421985.1:p.Thr109 0Ala

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5:131651842:G:A	missense	ENST00000510461.6:c.3266C>T	ENSP00000421985.1:p.Ser108 9Phe
5:131651842:G:T	missense	ENST00000510461.6:c.3266C>A	ENSP00000421985.1:p.Ser108 9Tyr
5:131651844:A:T	missense	ENST00000510461.6:c.3264T>A	ENSP00000421985.1:p.His108 8Gln
5:131651849:G:A	missense	ENST00000510461.6:c.3259C>T	ENSP00000421985.1:p.Leu108 7Phe
5:131651854:T:C	missense	ENST00000510461.6:c.3254A>G	ENSP00000421985.1:p.Asn108 5Ser
5:131651863:A:G	missense	ENST00000510461.6:c.3245T>C	ENSP00000421985.1:p.Leu108 2Pro
5:131651866:C:A	missense	ENST00000510461.6:c.3242G>T	ENSP00000421985.1:p.Ser108 1Ile
5:131651875:A:G	missense	ENST00000510461.6:c.3233T>C	ENSP00000421985.1:p.Leu107 8Ser
5:131651878:A:G	missense	ENST00000510461.6:c.3230T>C	ENSP00000421985.1:p.Val107 7Ala
5:131651879:C:T	missense	ENST00000510461.6:c.3229G>A	ENSP00000421985.1:p.Val107 7Ile
5:131651880:T:A	missense	ENST00000510461.6:c.3228A>T	ENSP00000421985.1:p.Glu107 6Asp
5:131651885:T:C	missense	ENST00000510461.6:c.3223A>G	ENSP00000421985.1:p.Lys107 5Glu
5:131651887:C:G	missense	ENST00000510461.6:c.3221G>C	ENSP00000421985.1:p.Gly107 4Ala
5:131651896:T:C	missense	ENST00000510461.6:c.3212A>G	ENSP00000421985.1:p.Asn107 1Ser
5:131651908:C:T	missense	ENST00000510461.6:c.3200G>A	ENSP00000421985.1:p.Arg106 7Gln
5:131651909:G:A	stop_gain ed	ENST00000510461.6:c.3199C>T	ENSP00000421985.1:p.Arg106 7Ter
5:131651909:G:C	missense	ENST00000510461.6:c.3199C>G	ENSP00000421985.1:p.Arg106 7Gly

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5:131651911:C:G	missense	ENST00000510461.6:c.3197G>C	ENSP00000421985.1:p.Arg106 6Thr
5:131651914:T:C	missense	ENST00000510461.6:c.3194A>G	ENSP00000421985.1:p.Gln106 5Arg
5:131651921:T:C	missense	ENST00000510461.6:c.3187A>G	ENSP00000421985.1:p.Ser106 3Gly
5:131651927:C:T	missense	ENST00000510461.6:c.3181G>A	ENSP00000421985.1:p.Val106 1Met
5:131651930:G:A	stop_gain ed	ENST00000510461.6:c.3178C>T	ENSP00000421985.1:p.Gln106 0Ter
5:131651930:G:C	missense	ENST00000510461.6:c.3178C>G	ENSP00000421985.1:p.Gln106 0Glu
5:131651930:GA: G	frameshif t	ENST00000510461.6:c.3177del	ENSP00000421985.1:p.Gln106 0LysfsTer9
5:131651933:C:T	missense	ENST00000510461.6:c.3175G>A	ENSP00000421985.1:p.Val105 9Ile
5:131651935:G:C	missense	ENST00000510461.6:c.3173C>G	ENSP00000421985.1:p.Thr105 8Ser
5:131651944:T:C	missense	ENST00000510461.6:c.3164A>G	ENSP00000421985.1:p.Asp105 5Gly
5:131651946:C:T	missense	ENST00000510461.6:c.3162G>A	ENSP00000421985.1:p.Met10 54Ile
5:131651947:A:C	missense	ENST00000510461.6:c.3161T>G	ENSP00000421985.1:p.Met10 54Arg
5:131651947:A:G	missense	ENST00000510461.6:c.3161T>C	ENSP00000421985.1:p.Met10 54Thr
5:131651948:T:C	missense	ENST00000510461.6:c.3160A>G	ENSP00000421985.1:p.Met10 54Val
5:131651956:A:G	missense	ENST00000510461.6:c.3152T>C	ENSP00000421985.1:p.Ile1051 Thr
5:131651963:A:G	missense	ENST00000510461.6:c.3145T>C	ENSP00000421985.1:p.Cys104 9Arg
5:131651963:A:T	missense	ENST00000510461.6:c.3145T>A	ENSP00000421985.1:p.Cys104 9Ser

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5:131651966:C:G	missense	ENST00000510461.6:c.3142G>C	ENSP00000421985.1:p.Val104 8Leu
5:131651966:C:T	missense	ENST00000510461.6:c.3142G>A	ENSP00000421985.1:p.Val104 8Ile
5:131651968:G:C	missense	ENST00000510461.6:c.3140C>G	ENSP00000421985.1:p.Ala104 7Gly
5:131651969:C:T	missense	ENST00000510461.6:c.3139G>A	ENSP00000421985.1:p.Ala104 7Thr
5:131651972:C:T	missense	ENST00000510461.6:c.3136G>A	ENSP00000421985.1:p.Glu104 6Lys
5:131651978:T:C	missense	ENST00000510461.6:c.3130A>G	ENSP00000421985.1:p.Ile1044 Val
5:131651993:C:G	missense	ENST00000510461.6:c.3115G>C	ENSP00000421985.1:p.Val103 9Leu
5:131651995:G:A	missense	ENST00000510461.6:c.3113C>T	ENSP00000421985.1:p.Pro103 8Leu
5:131651999:G:T	missense	ENST00000510461.6:c.3109C>A	ENSP00000421985.1:p.His103 7Asn
5:131670467:A:G	missense	ENST00000510461.6:c.3104T>C	ENSP00000421985.1:p.Val103 5Ala
5:131670468:C:T	missense	ENST00000510461.6:c.3103G>A	ENSP00000421985.1:p.Val103 5Met
5:131670471:C:T	missense	ENST00000510461.6:c.3100G>A	ENSP00000421985.1:p.Ala103 4Thr
5:131670472:A:T	missense	ENST00000510461.6:c.3099T>A	ENSP00000421985.1:p.His103 3Gln
5:131670473:T:C	missense	ENST00000510461.6:c.3098A>G	ENSP00000421985.1:p.His103 3Arg
5:131670473:T:G	missense	ENST00000510461.6:c.3098A>C	ENSP00000421985.1:p.His103 3Pro
5:131670474:G:T	missense	ENST00000510461.6:c.3097C>A	ENSP00000421985.1:p.His103 3Asn
5:131670476:G:A	missense	ENST00000510461.6:c.3095C>T	ENSP00000421985.1:p.Ser103 2Phe

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5:131670476:G:C	missense	ENST00000510461.6:c.3095C>G	ENSP00000421985.1:p.Ser103 2Cys
5:131670477:A:C	missense	ENST00000510461.6:c.3094T>G	ENSP00000421985.1:p.Ser103 2Ala
5:131670482:T:A	missense	ENST00000510461.6:c.3089A>T	ENSP00000421985.1:p.Asp103 0Val
5:131670483:C:G	missense	ENST00000510461.6:c.3088G>C	ENSP00000421985.1:p.Asp103 0His
5:131670483:C:T	missense	ENST00000510461.6:c.3088G>A	ENSP00000421985.1:p.Asp103 0Asn
5:131670487:C:T	missense	ENST00000510461.6:c.3084G>A	ENSP00000421985.1:p.Met10 28Ile
5:131670493:A:T	stop_gain ed	ENST00000510461.6:c.3078T>A	ENSP00000421985.1:p.Cys102 6Ter
5:131670500:C:A	missense	ENST00000510461.6:c.3071G>T	ENSP00000421985.1:p.Arg102 4Leu
5:131670500:C:T	missense	ENST00000510461.6:c.3071G>A	ENSP00000421985.1:p.Arg102 4His
5:131670501:G:A	missense	ENST00000510461.6:c.3070C>T	ENSP00000421985.1:p.Arg102 4Cys
5:131670502:G:C	missense	ENST00000510461.6:c.3069C>G	ENSP00000421985.1:p.Phe10 23Leu
5:131670503:A:T	missense	ENST00000510461.6:c.3068T>A	ENSP00000421985.1:p.Phe10 23Tyr
5:131670505:C:G	missense	ENST00000510461.6:c.3066G>C	ENSP00000421985.1:p.Arg102 2Ser
5:131670506:C:T	missense	ENST00000510461.6:c.3065G>A	ENSP00000421985.1:p.Arg102 2Lys
5:131670510:C:T	missense	ENST00000510461.6:c.3061G>A	ENSP00000421985.1:p.Glu102 1Lys
5:131670511:A:C	missense	ENST00000510461.6:c.3060T>G	ENSP00000421985.1:p.Asp102 0Glu
5:131670514:A:C	missense	ENST00000510461.6:c.3057T>G	ENSP00000421985.1:p.Ser101 9Arg

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5:131670519:C:A	missense	ENST00000510461.6:c.3052G>T	ENSP00000421985.1:p.Gly101 8Trp
5:131670521:A:G	missense	ENST00000510461.6:c.3050T>C	ENSP00000421985.1:p.Ile1017 Thr
5:131670540:C:G	missense	ENST00000510461.6:c.3031G>C	ENSP00000421985.1:p.Asp101 1His
5:131670543:G:T	missense	ENST00000510461.6:c.3028C>A	ENSP00000421985.1:p.Pro101 0Thr
5:131670546:C:T	missense	ENST00000510461.6:c.3025G>A	ENSP00000421985.1:p.Val100 9Met
5:131670550:A:A T	frameshift	ENST00000510461.6:c.3020_30 21insA	ENSP00000421985.1:p.Tyr100 8LeufsTer4
5:131670551:G:A	missense	ENST00000510461.6:c.3020C>T	ENSP00000421985.1:p.Ser100 7Phe
5:131670552:A:G	missense	ENST00000510461.6:c.3019T>C	ENSP00000421985.1:p.Ser100 7Pro
5:131670554:G:A	missense	ENST00000510461.6:c.3017C>T	ENSP00000421985.1:p.Ser100 6Leu
5:131670554:G:T	stop_gained	ENST00000510461.6:c.3017C>A	ENSP00000421985.1:p.Ser100 6Ter
5:131670560:T:C	missense	ENST00000510461.6:c.3011A>G	ENSP00000421985.1:p.Tyr100 4Cys
5:131670561:A:G	missense	ENST00000510461.6:c.3010T>C	ENSP00000421985.1:p.Tyr100 4His
5:131670579:T:A	missense	ENST00000510461.6:c.2992A>T	ENSP00000421985.1:p.Arg998 Trp
5:131670582:C:T	missense	ENST00000510461.6:c.2989G>A	ENSP00000421985.1:p.Gly997 Arg
5:131670585:A:G	missense	ENST00000510461.6:c.2986T>C	ENSP00000421985.1:p.Phe99 6Leu
5:131670593:A:G	missense	ENST00000510461.6:c.2978T>C	ENSP00000421985.1:p.Ile993T hr
5:131670594:T:C	missense	ENST00000510461.6:c.2977A>G	ENSP00000421985.1:p.Ile993 Val

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5:131670596:T:A	missense	ENST00000510461.6:c.2975A>T	ENSP00000421985.1:p.Asn992 Ile
5:131670605:A:T	missense	ENST00000510461.6:c.2966T>A	ENSP00000421985.1:p.Val989 Asp
5:131670606:C:G	missense	ENST00000510461.6:c.2965G>C	ENSP00000421985.1:p.Val989 Leu
5:131670606:C:T	missense	ENST00000510461.6:c.2965G>A	ENSP00000421985.1:p.Val989 Ile
5:131670610:A:C	missense	ENST00000510461.6:c.2961T>G	ENSP00000421985.1:p.Ser987 Arg
5:131670611:C:A	missense	ENST00000510461.6:c.2960G>T	ENSP00000421985.1:p.Ser987 Ile
5:131670611:C:T	missense	ENST00000510461.6:c.2960G>A	ENSP00000421985.1:p.Ser987 Asn
5:131670612:T:C	missense	ENST00000510461.6:c.2959A>G	ENSP00000421985.1:p.Ser987 Gly
5:131670614:A:G	missense	ENST00000510461.6:c.2957T>C	ENSP00000421985.1:p.Val986 Ala
5:131670618:C:T	missense	ENST00000510461.6:c.2953G>A	ENSP00000421985.1:p.Glu985 Lys
5:131670621:T:C	missense	ENST00000510461.6:c.2950A>G	ENSP00000421985.1:p.Ile984 Val
5:131670626:T:C	missense	ENST00000510461.6:c.2945A>G	ENSP00000421985.1:p.Lys982 Arg
5:131670632:C:T	splice_acc eptor	ENST00000510461.6:c.2940- 1G>A	NA
5:131671506:C:A	missense	ENST00000510461.6:c.2938G>T	ENSP00000421985.1:p.Gly980 Trp
5:131671509:G:A	missense	ENST00000510461.6:c.2935C>T	ENSP00000421985.1:p.Pro979 Ser
5:131671509:G:C	missense	ENST00000510461.6:c.2935C>G	ENSP00000421985.1:p.Pro979 Ala
5:131671514:G:C	missense	ENST00000510461.6:c.2930C>G	ENSP00000421985.1:p.Pro977 Arg

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5:131671516:T:C	missense	ENST00000510461.6:c.2928A>G	ENSP00000421985.1:p.Ile976 Met
5:131671522:A:C	missense	ENST00000510461.6:c.2922T>G	ENSP00000421985.1:p.Asp974 Glu
5:131671522:A:T	missense	ENST00000510461.6:c.2922T>A	ENSP00000421985.1:p.Asp974 Glu
5:131671524:C:T	missense	ENST00000510461.6:c.2920G>A	ENSP00000421985.1:p.Asp974 Asn
5:131671527:C:T	missense	ENST00000510461.6:c.2917G>A	ENSP00000421985.1:p.Glu973 Lys
5:131671533:C:A	missense	ENST00000510461.6:c.2911G>T	ENSP00000421985.1:p.Ala971 Ser
5:131671533:C:G	missense	ENST00000510461.6:c.2911G>C	ENSP00000421985.1:p.Ala971 Pro
5:131671533:C:T	missense	ENST00000510461.6:c.2911G>A	ENSP00000421985.1:p.Ala971 Thr
5:131671534:C:A	missense	ENST00000510461.6:c.2910G>T	ENSP00000421985.1:p.Trp970 Cys
5:131671538:T:A	missense	ENST00000510461.6:c.2906A>T	ENSP00000421985.1:p.Asp969 Val
5:131671539:C:G	missense	ENST00000510461.6:c.2905G>C	ENSP00000421985.1:p.Asp969 His
5:131671543:T:G	missense	ENST00000510461.6:c.2901A>C	ENSP00000421985.1:p.Gln967 His
5:131671545:G:C	missense	ENST00000510461.6:c.2899C>G	ENSP00000421985.1:p.Gln967 Glu
5:131671548:C:G	missense	ENST00000510461.6:c.2896G>C	ENSP00000421985.1:p.Glu966 Gln
5:131671551:C:T	missense	ENST00000510461.6:c.2893G>A	ENSP00000421985.1:p.Gly965 Arg
5:131671554:C:T	missense	ENST00000510461.6:c.2890G>A	ENSP00000421985.1:p.Gly964 Arg
5:131671557:A:C	missense	ENST00000510461.6:c.2887T>G	ENSP00000421985.1:p.Tyr963 Asp

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5:131671559:T:C	missense	ENST00000510461.6:c.2885A>G	ENSP00000421985.1:p.Tyr962 Cys
5:131671562:C:T	missense	ENST00000510461.6:c.2882G>A	ENSP00000421985.1:p.Ser961 Asn
5:131671569:C:T	missense	ENST00000510461.6:c.2875G>A	ENSP00000421985.1:p.Val959I Ile
5:131671572:G:C	missense	ENST00000510461.6:c.2872C>G	ENSP00000421985.1:p.Gln958 Glu
5:131671572:G:T	missense	ENST00000510461.6:c.2872C>A	ENSP00000421985.1:p.Gln958 Lys
5:131671574:C:T	missense	ENST00000510461.6:c.2870G>A	ENSP00000421985.1:p.Arg957 Lys
5:131671575:T:C	missense	ENST00000510461.6:c.2869A>G	ENSP00000421985.1:p.Arg957 Gly
5:131671584:C:T	missense	ENST00000510461.6:c.2860G>A	ENSP00000421985.1:p.Asp954 Asn
5:131671586:T:C	missense	ENST00000510461.6:c.2858A>G	ENSP00000421985.1:p.His953 Arg
5:131671589:C:A	missense	ENST00000510461.6:c.2855G>T	ENSP00000421985.1:p.Gly952 Val
5:131671592:G:A	missense	ENST00000510461.6:c.2852C>T	ENSP00000421985.1:p.Thr951 Ile
5:131671595:T:C	missense	ENST00000510461.6:c.2849A>G	ENSP00000421985.1:p.Asp950 Gly
5:131671595:T:G	missense	ENST00000510461.6:c.2849A>C	ENSP00000421985.1:p.Asp950 Ala
5:131671601:C:T	missense	ENST00000510461.6:c.2843G>A	ENSP00000421985.1:p.Ser948 Asn
5:131671604:T:C	missense	ENST00000510461.6:c.2840A>G	ENSP00000421985.1:p.Glu947 Gly
5:131671604:T:G	missense	ENST00000510461.6:c.2840A>C	ENSP00000421985.1:p.Glu947 Ala
5:131671610:T:C	missense	ENST00000510461.6:c.2834A>G	ENSP00000421985.1:p.Asp945 Gly

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5:131671610:T:G	missense	ENST00000510461.6:c.2834A>C	ENSP00000421985.1:p.Asp945 Ala
5:131671613:C:T	missense	ENST00000510461.6:c.2831G>A	ENSP00000421985.1:p.Gly944 Glu
5:131671614:C:T	missense	ENST00000510461.6:c.2830G>A	ENSP00000421985.1:p.Gly944 Arg
5:131671617:G:A	missense	ENST00000510461.6:c.2827C>T	ENSP00000421985.1:p.Leu943 Phe
5:131671628:G:A	missense	ENST00000510461.6:c.2816C>T	ENSP00000421985.1:p.Ser939 Leu
5:131671632:T:C	missense	ENST00000510461.6:c.2812A>G	ENSP00000421985.1:p.Ser938 Gly
5:131671634:T:C	missense	ENST00000510461.6:c.2810A>G	ENSP00000421985.1:p.Glu937 Gly
5:131671634:T:G	missense	ENST00000510461.6:c.2810A>C	ENSP00000421985.1:p.Glu937 Ala
5:131671639:T:G	missense	ENST00000510461.6:c.2805A>C	ENSP00000421985.1:p.Arg935 Ser
5:131671646:A:T	missense	ENST00000510461.6:c.2798T>A	ENSP00000421985.1:p.Ile933 Asn
5:131671647:T:A	missense	ENST00000510461.6:c.2797A>T	ENSP00000421985.1:p.Ile933P he
5:131671647:T:C	missense	ENST00000510461.6:c.2797A>G	ENSP00000421985.1:p.Ile933 Val
5:131671647:T:G	missense	ENST00000510461.6:c.2797A>C	ENSP00000421985.1:p.Ile933L eu
5:131671658:G:A	missense	ENST00000510461.6:c.2786C>T	ENSP00000421985.1:p.Thr929 Ile
5:131671658:G:C	missense	ENST00000510461.6:c.2786C>G	ENSP00000421985.1:p.Thr929 Ser
5:131671659:T:C	missense	ENST00000510461.6:c.2785A>G	ENSP00000421985.1:p.Thr929 Ala
5:131671661:C:T	missense	ENST00000510461.6:c.2783G>A	ENSP00000421985.1:p.Gly928 Glu

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5:131671664:A:C	missense	ENST00000510461.6:c.2780T>G	ENSP00000421985.1:p.Val927 Gly
5:131671665:C:T	missense	ENST00000510461.6:c.2779G>A	ENSP00000421985.1:p.Val927I le
5:131671668:C:A	missense	ENST00000510461.6:c.2776G>T	ENSP00000421985.1:p.Ala926 Ser
5:131671669:A:C	missense	ENST00000510461.6:c.2775T>G	ENSP00000421985.1:p.Ile925 Met
5:131671670:A:A T	frameshift	ENST00000510461.6:c.2773dup	ENSP00000421985.1:p.Ile925 AsnfsTer6
5:131671670:A:T	missense	ENST00000510461.6:c.2774T>A	ENSP00000421985.1:p.Ile925 Asn
5:131671673:T:C	missense	ENST00000510461.6:c.2771A>G	ENSP00000421985.1:p.Lys924 Arg
5:131671677:T:A	stop_gained	ENST00000510461.6:c.2767A>T	ENSP00000421985.1:p.Lys923 Ter
5:131671680:C:T	missense	ENST00000510461.6:c.2764G>A	ENSP00000421985.1:p.Asp922 Asn
5:131671683:A:C	missense	ENST00000510461.6:c.2761T>G	ENSP00000421985.1:p.Ser921 Ala
5:131671685:C:A	missense	ENST00000510461.6:c.2759G>T	ENSP00000421985.1:p.Ser920 Ile
5:131671686:T:C	missense	ENST00000510461.6:c.2758A>G	ENSP00000421985.1:p.Ser920 Gly
5:131671691:T:C	missense	ENST00000510461.6:c.2753A>G	ENSP00000421985.1:p.Lys918 Arg
5:131671692:T:C	missense	ENST00000510461.6:c.2752A>G	ENSP00000421985.1:p.Lys918 Glu
5:131671694:T:A	missense	ENST00000510461.6:c.2750A>T	ENSP00000421985.1:p.Asp917 Val
5:131671697:C:A	missense	ENST00000510461.6:c.2747G>T	ENSP00000421985.1:p.Gly916 Val
5:131671700:T:C	missense	ENST00000510461.6:c.2744A>G	ENSP00000421985.1:p.His915 Arg

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5:131671700:TG: T	frameshif t	ENST00000510461.6:c.2743del	ENSP00000421985.1:p.His915 MetfsTer13
5:131671701:G:A	missense	ENST00000510461.6:c.2743C>T	ENSP00000421985.1:p.His915 Tyr
5:131671703:G:A	missense	ENST00000510461.6:c.2741C>T	ENSP00000421985.1:p.Pro914 Leu
5:131671703:G:C	missense	ENST00000510461.6:c.2741C>G	ENSP00000421985.1:p.Pro914 Arg
5:131671704:G:A	missense	ENST00000510461.6:c.2740C>T	ENSP00000421985.1:p.Pro914 Ser
5:131671705:GA: G	frameshif t	ENST00000510461.6:c.2738del	ENSP00000421985.1:p.Val913 AlafsTer15
5:131671706:A:T	missense	ENST00000510461.6:c.2738T>A	ENSP00000421985.1:p.Val913 Asp
5:131671710:G:T	missense	ENST00000510461.6:c.2734C>A	ENSP00000421985.1:p.Leu912 Ile
5:131671712:A:C	missense	ENST00000510461.6:c.2732T>G	ENSP00000421985.1:p.Ile911S er
5:131671713:T:C	missense	ENST00000510461.6:c.2731A>G	ENSP00000421985.1:p.Ile911 Val
5:131671713:TG: T	frameshif t	ENST00000510461.6:c.2730del	ENSP00000421985.1:p.Ile911P hefsTer17
5:131671718:A:G	missense	ENST00000510461.6:c.2726T>C	ENSP00000421985.1:p.Leu909 Pro
5:131671718:A:T	missense	ENST00000510461.6:c.2726T>A	ENSP00000421985.1:p.Leu909 His
5:131671726:T:A	missense	ENST00000510461.6:c.2718A>T	ENSP00000421985.1:p.Arg906 Ser
5:131671732:G:C	missense	ENST00000510461.6:c.2712C>G	ENSP00000421985.1:p.Asp904 Glu
5:131671734:C:T	missense	ENST00000510461.6:c.2710G>A	ENSP00000421985.1:p.Asp904 Asn
5:131671740:G:C	missense	ENST00000510461.6:c.2704C>G	ENSP00000421985.1:p.Gln902 Glu

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5:131671742:G:A	missense	ENST00000510461.6:c.2702C>T	ENSP00000421985.1:p.Pro901 Leu
5:131671742:G:T	missense	ENST00000510461.6:c.2702C>A	ENSP00000421985.1:p.Pro901 His
5:131671745:A:G	missense	ENST00000510461.6:c.2699T>C	ENSP00000421985.1:p.Phe90 OSer
5:131671751:G:A	missense	ENST00000510461.6:c.2693C>T	ENSP00000421985.1:p.Thr898 Ile
5:131671751:G:T	missense	ENST00000510461.6:c.2693C>A	ENSP00000421985.1:p.Thr898 Asn
5:131671754:T:C	missense	ENST00000510461.6:c.2690A>G	ENSP00000421985.1:p.Lys897 Arg
5:131671755:T:A	stop_gain ed	ENST00000510461.6:c.2689A>T	ENSP00000421985.1:p.Lys897 Ter
5:131671758:A:G	missense	ENST00000510461.6:c.2686T>C	ENSP00000421985.1:p.Cys896 Arg
5:131671760:G:A	missense	ENST00000510461.6:c.2684C>T	ENSP00000421985.1:p.Ser895 Leu
5:131671761:A:T	missense	ENST00000510461.6:c.2683T>A	ENSP00000421985.1:p.Ser895 Thr
5:131671762:A:C	missense	ENST00000510461.6:c.2682T>G	ENSP00000421985.1:p.Asp894 Glu
5:131671763:T:C	missense	ENST00000510461.6:c.2681A>G	ENSP00000421985.1:p.Asp894 Gly
5:131671764:C:G	missense	ENST00000510461.6:c.2680G>C	ENSP00000421985.1:p.Asp894 His
5:131671764:C:T	missense	ENST00000510461.6:c.2680G>A	ENSP00000421985.1:p.Asp894 Asn
5:131671767:G:C	missense	ENST00000510461.6:c.2677C>G	ENSP00000421985.1:p.Gln893 Glu
5:131671769:G:A	missense	ENST00000510461.6:c.2675C>T	ENSP00000421985.1:p.Pro892 Leu
5:131671770:G:A	missense	ENST00000510461.6:c.2674C>T	ENSP00000421985.1:p.Pro892 Ser

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5:131671770:G:T	missense	ENST00000510461.6:c.2674C>A	ENSP00000421985.1:p.Pro892 Thr
5:131671772:A:C	missense	ENST00000510461.6:c.2672T>G	ENSP00000421985.1:p.Val891 Gly
5:131671772:A:G	missense	ENST00000510461.6:c.2672T>C	ENSP00000421985.1:p.Val891 Ala
5:131671773:C:A	missense	ENST00000510461.6:c.2671G>T	ENSP00000421985.1:p.Val891 Phe
5:131671775:G:A	missense	ENST00000510461.6:c.2669C>T	ENSP00000421985.1:p.Thr890 Ile
5:131671776:T:C	missense	ENST00000510461.6:c.2668A>G	ENSP00000421985.1:p.Thr890 Ala
5:131671778:T:C	missense	ENST00000510461.6:c.2666A>G	ENSP00000421985.1:p.Glu889 Gly
5:131671779:C:G	missense	ENST00000510461.6:c.2665G>C	ENSP00000421985.1:p.Glu889 Gln
5:131671779:C:T	missense	ENST00000510461.6:c.2665G>A	ENSP00000421985.1:p.Glu889 Lys
5:131671780:T:C	missense	ENST00000510461.6:c.2664A>G	ENSP00000421985.1:p.Ile888 Met
5:131671782:T:C	missense	ENST00000510461.6:c.2662A>G	ENSP00000421985.1:p.Ile888 Val
5:131671784:C:T	missense	ENST00000510461.6:c.2660G>A	ENSP00000421985.1:p.Cys887 Tyr
5:131671788:T:G	missense	ENST00000510461.6:c.2656A>C	ENSP00000421985.1:p.Lys886 Gln
5:131671788:TA: T	frameshift	ENST00000510461.6:c.2655del	ENSP00000421985.1:p.Cys885 Ter
5:131671794:A:G	missense	ENST00000510461.6:c.2650T>C	ENSP00000421985.1:p.Phe88 4Leu
5:131671795:T:A	missense	ENST00000510461.6:c.2649A>T	ENSP00000421985.1:p.Glu883 Asp
5:131671796:T:C	missense	ENST00000510461.6:c.2648A>G	ENSP00000421985.1:p.Glu883 Gly

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5:131671797:C:G	missense	ENST00000510461.6:c.2647G>C	ENSP00000421985.1:p.Glu883 Gln
5:131671797:C:T	missense	ENST00000510461.6:c.2647G>A	ENSP00000421985.1:p.Glu883 Lys
5:131671798:A:T	missense	ENST00000510461.6:c.2646T>A	ENSP00000421985.1:p.Asn882 Lys
5:131671802:T:A	missense	ENST00000510461.6:c.2642A>T	ENSP00000421985.1:p.Asn881 Ile
5:131671802:T:C	missense	ENST00000510461.6:c.2642A>G	ENSP00000421985.1:p.Asn881 Ser
5:131671812:T:C	missense	ENST00000510461.6:c.2632A>G	ENSP00000421985.1:p.Asn878 Asp
5:131671814:T:A	missense	ENST00000510461.6:c.2630A>T	ENSP00000421985.1:p.Asn877 Ile
5:131671814:T:C	missense	ENST00000510461.6:c.2630A>G	ENSP00000421985.1:p.Asn877 Ser
5:131671816:T:G	missense	ENST00000510461.6:c.2628A>C	ENSP00000421985.1:p.Lys876 Asn
5:131671821:T:C	missense	ENST00000510461.6:c.2623A>G	ENSP00000421985.1:p.Thr875 Ala
5:131671823:C:T	missense	ENST00000510461.6:c.2621G>A	ENSP00000421985.1:p.Cys874 Tyr
5:131671825:C:A	missense	ENST00000510461.6:c.2619G>T	ENSP00000421985.1:p.Leu873 Phe
5:131671825:C:G	missense	ENST00000510461.6:c.2619G>C	ENSP00000421985.1:p.Leu873 Phe
5:131671832:T:G	missense	ENST00000510461.6:c.2612A>C	ENSP00000421985.1:p.Lys871 Thr
5:131671842:C:G	missense	ENST00000510461.6:c.2602G>C	ENSP00000421985.1:p.Glu868 Gln
5:131671844:A:G	missense	ENST00000510461.6:c.2600T>C	ENSP00000421985.1:p.Leu867 Ser
5:131671846:C:T	missense	ENST00000510461.6:c.2598G>A	ENSP00000421985.1:p.Met86 Ile

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5:131671847:A:G	missense	ENST00000510461.6:c.2597T>C	ENSP00000421985.1:p.Met86 6Thr
5:131671847:A:T	missense	ENST00000510461.6:c.2597T>A	ENSP00000421985.1:p.Met86 6Lys
5:131671848:T:C	missense	ENST00000510461.6:c.2596A>G	ENSP00000421985.1:p.Met86 6Val
5:131671850:C:T	missense	ENST00000510461.6:c.2594G>A	ENSP00000421985.1:p.Cys865 Tyr
5:131671851:A:T	missense	ENST00000510461.6:c.2593T>A	ENSP00000421985.1:p.Cys865 Ser
5:131671853:C:T	missense	ENST00000510461.6:c.2591G>A	ENSP00000421985.1:p.Cys864 Tyr
5:131671854:A:T	missense	ENST00000510461.6:c.2590T>A	ENSP00000421985.1:p.Cys864 Ser
5:131671860:C:G	missense	ENST00000510461.6:c.2584G>C	ENSP00000421985.1:p.Asp862 His
5:131671866:T:C	missense	ENST00000510461.6:c.2578A>G	ENSP00000421985.1:p.Ser860 Gly
5:131671867:A:T	missense	ENST00000510461.6:c.2577T>A	ENSP00000421985.1:p.Asp859 Glu
5:131671868:T:C	missense	ENST00000510461.6:c.2576A>G	ENSP00000421985.1:p.Asp859 Gly
5:131671869:C:T	missense	ENST00000510461.6:c.2575G>A	ENSP00000421985.1:p.Asp859 Asn
5:131671874:C:T	missense	ENST00000510461.6:c.2570G>A	ENSP00000421985.1:p.Ser857 Asn
5:131671878:T:C	missense	ENST00000510461.6:c.2566A>G	ENSP00000421985.1:p.Thr856 Ala
5:131671882:A:T	missense	ENST00000510461.6:c.2562T>A	ENSP00000421985.1:p.Phe85 4Leu
5:131671887:G:C	missense	ENST00000510461.6:c.2557C>G	ENSP00000421985.1:p.Pro853 Ala
5:131671889:A:G	missense	ENST00000510461.6:c.2555T>C	ENSP00000421985.1:p.Val852 Ala

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5:131671889:A:T	missense	ENST00000510461.6:c.2555T>A	ENSP00000421985.1:p.Val852 Asp
5:131671890:C:A	missense	ENST00000510461.6:c.2554G>T	ENSP00000421985.1:p.Val852 Phe
5:131671895:T:A	missense	ENST00000510461.6:c.2549A>T	ENSP00000421985.1:p.Asp850 Val
5:131671896:C:T	missense	ENST00000510461.6:c.2548G>A	ENSP00000421985.1:p.Asp850 Asn
5:131671899:T:C	missense	ENST00000510461.6:c.2545A>G	ENSP00000421985.1:p.Ile849 Val
5:131671899:T:T A	frameshift	ENST00000510461.6:c.2544dup	ENSP00000421985.1:p.Ile849T yrfsTer2
5:131671905:T:C	missense	ENST00000510461.6:c.2539A>G	ENSP00000421985.1:p.Arg847 Gly
5:131671907:G:A	missense	ENST00000510461.6:c.2537C>T	ENSP00000421985.1:p.Thr846 Ile
5:131671908:T:C	missense	ENST00000510461.6:c.2536A>G	ENSP00000421985.1:p.Thr846 Ala
5:131671908:T:G	missense	ENST00000510461.6:c.2536A>C	ENSP00000421985.1:p.Thr846 Pro
5:131671911:C:T	missense	ENST00000510461.6:c.2533G>A	ENSP00000421985.1:p.Glu845 Lys
5:131671912:G:C	missense	ENST00000510461.6:c.2532C>G	ENSP00000421985.1:p.Ile844 Met
5:131671914:T:C	missense	ENST00000510461.6:c.2530A>G	ENSP00000421985.1:p.Ile844 Val
5:131671918:A:C	missense	ENST00000510461.6:c.2526T>G	ENSP00000421985.1:p.Asp842 Glu
5:131671922:T:A	missense	ENST00000510461.6:c.2522A>T	ENSP00000421985.1:p.Asp841 Val
5:131671922:T:C	missense	ENST00000510461.6:c.2522A>G	ENSP00000421985.1:p.Asp841 Gly
5:131671924:A:T	missense	ENST00000510461.6:c.2520T>A	ENSP00000421985.1:p.Asn840 Lys

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5:131671925:T:C	missense	ENST00000510461.6:c.2519A>G	ENSP00000421985.1:p.Asn840 Ser
5:131671926:T:G	missense	ENST00000510461.6:c.2518A>C	ENSP00000421985.1:p.Asn840 His
5:131671928:A:G	missense	ENST00000510461.6:c.2516T>C	ENSP00000421985.1:p.Phe83 9Ser
5:131671933:T:A	missense	ENST00000510461.6:c.2511A>T	ENSP00000421985.1:p.Glu837 Asp
5:131671935:C:T	missense	ENST00000510461.6:c.2509G>A	ENSP00000421985.1:p.Glu837 Lys
5:131671938:C:T	missense	ENST00000510461.6:c.2506G>A	ENSP00000421985.1:p.Asp836 Asn
5:131671939:G:C	missense	ENST00000510461.6:c.2505C>G	ENSP00000421985.1:p.Phe83 5Leu
5:131671941:A:G	missense	ENST00000510461.6:c.2503T>C	ENSP00000421985.1:p.Phe83 5Leu
5:131671946:C:T	missense	ENST00000510461.6:c.2498G>A	ENSP00000421985.1:p.Ser833 Asn
5:131671950:T:C	missense	ENST00000510461.6:c.2494A>G	ENSP00000421985.1:p.Met83 2Val
5:131671954:T:G	missense	ENST00000510461.6:c.2490A>C	ENSP00000421985.1:p.Glu830 Asp
5:131671956:C:T	missense	ENST00000510461.6:c.2488G>A	ENSP00000421985.1:p.Glu830 Lys
5:131671959:G:C	missense	ENST00000510461.6:c.2485C>G	ENSP00000421985.1:p.Pro829 Ala
5:131671963:TG: T	frameshift	ENST00000510461.6:c.2480del	ENSP00000421985.1:p.Ser827 Ter
5:131671964:G:A	missense	ENST00000510461.6:c.2480C>T	ENSP00000421985.1:p.Ser827 Leu
5:131671965:A:C	missense	ENST00000510461.6:c.2479T>G	ENSP00000421985.1:p.Ser827 Ala
5:131671967:T:C	missense	ENST00000510461.6:c.2477A>G	ENSP00000421985.1:p.His826 Arg

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5:131671969:ATT CC:A	frameshift	ENST00000510461.6:c.2471_2474del	ENSP00000421985.1:p.Trp824 PhefsTer8
5:131671970:T:C	missense	ENST00000510461.6:c.2474A>G	ENSP00000421985.1:p.Asn825 Ser
5:131671979:G:A	missense	ENST00000510461.6:c.2465C>T	ENSP00000421985.1:p.Pro822 Leu
5:131671980:G:C	missense	ENST00000510461.6:c.2464C>G	ENSP00000421985.1:p.Pro822 Ala
5:131671988:C:T	missense	ENST00000510461.6:c.2456G>A	ENSP00000421985.1:p.Cys819 Tyr
5:131671991:G:A	missense	ENST00000510461.6:c.2453C>T	ENSP00000421985.1:p.Pro818 Leu
5:131671992:G:T	missense	ENST00000510461.6:c.2452C>A	ENSP00000421985.1:p.Pro818 Thr
5:131671997:T:G	missense	ENST00000510461.6:c.2447A>C	ENSP00000421985.1:p.Glu816 Ala
5:131671998:C:T	missense	ENST00000510461.6:c.2446G>A	ENSP00000421985.1:p.Glu816 Lys
5:131672000:G:A	missense	ENST00000510461.6:c.2444C>T	ENSP00000421985.1:p.Ser815 Phe
5:131672003:A:G	missense	ENST00000510461.6:c.2441T>C	ENSP00000421985.1:p.Val814 Ala
5:131672004:C:T	missense	ENST00000510461.6:c.2440G>A	ENSP00000421985.1:p.Val814 Ile
5:131672024:T:C	missense	ENST00000510461.6:c.2420A>G	ENSP00000421985.1:p.Glu807 Gly
5:131672025:C:C TCCAGATTGG	frameshift	ENST00000510461.6:c.2409_2418dup	ENSP00000421985.1:p.Glu807 ProfsTer6
5:131672027:C:T	missense	ENST00000510461.6:c.2417G>A	ENSP00000421985.1:p.Gly806 Glu
5:131672028:C:G	missense	ENST00000510461.6:c.2416G>C	ENSP00000421985.1:p.Gly806 Arg
5:131672030:G:C	missense	ENST00000510461.6:c.2414C>G	ENSP00000421985.1:p.Ser805 Cys

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5:131672031:A:G	missense	ENST00000510461.6:c.2413T>C	ENSP00000421985.1:p.Ser805 Pro
5:131672032:T:G	missense	ENST00000510461.6:c.2412A>C	ENSP00000421985.1:p.Gln804 His
5:131672033:TGG TCC:T	frameshift	ENST00000510461.6:c.2406_24 10del	ENSP00000421985.1:p.Asp803 IlefsTer5
5:131672036:T:C	missense	ENST00000510461.6:c.2408A>G	ENSP00000421985.1:p.Asp803 Gly
5:131672037:C:T	missense	ENST00000510461.6:c.2407G>A	ENSP00000421985.1:p.Asp803 Asn
5:131672052:T:C	missense	ENST00000510461.6:c.2392A>G	ENSP00000421985.1:p.Lys798 Glu
5:131672054:G:A	missense	ENST00000510461.6:c.2390C>T	ENSP00000421985.1:p.Thr797 Ile
5:131672055:T:C	missense	ENST00000510461.6:c.2389A>G	ENSP00000421985.1:p.Thr797 Ala
5:131672055:T:G	missense	ENST00000510461.6:c.2389A>C	ENSP00000421985.1:p.Thr797 Pro
5:131672060:T:G	missense	ENST00000510461.6:c.2384A>C	ENSP00000421985.1:p.Gln795 Pro
5:131672062:A:T	missense	ENST00000510461.6:c.2382T>A	ENSP00000421985.1:p.His794 Gln
5:131672063:T:G	missense	ENST00000510461.6:c.2381A>C	ENSP00000421985.1:p.His794 Pro
5:131672064:G:A	missense	ENST00000510461.6:c.2380C>T	ENSP00000421985.1:p.His794 Tyr
5:131672064:G:T	missense	ENST00000510461.6:c.2380C>A	ENSP00000421985.1:p.His794 Asn
5:131672066:T:C	missense	ENST00000510461.6:c.2378A>G	ENSP00000421985.1:p.Gln793 Arg
5:131672067:G:A	stop_gained	ENST00000510461.6:c.2377C>T	ENSP00000421985.1:p.Gln793 Ter
5:131672067:G:T	missense	ENST00000510461.6:c.2377C>A	ENSP00000421985.1:p.Gln793 Lys

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5:131672070:C:T	missense	ENST00000510461.6:c.2374G>A	ENSP00000421985.1:p.Asp792 Asn
5:131672078:CCT :C	frameshift	ENST00000510461.6:c.2364_2365del	ENSP00000421985.1:p.Ala790 TyrfsTer2
5:131672086:T:G	missense	ENST00000510461.6:c.2358A>C	ENSP00000421985.1:p.Glu786 Asp
5:131672087:T:C	missense	ENST00000510461.6:c.2357A>G	ENSP00000421985.1:p.Glu786 Gly
5:131672088:C:T	missense	ENST00000510461.6:c.2356G>A	ENSP00000421985.1:p.Glu786 Lys
5:131672096:G:A	missense	ENST00000510461.6:c.2348C>T	ENSP00000421985.1:p.Pro783 Leu
5:131672097:G:A	missense	ENST00000510461.6:c.2347C>T	ENSP00000421985.1:p.Pro783 Ser
5:131672100:T:C	missense	ENST00000510461.6:c.2344A>G	ENSP00000421985.1:p.Lys782 Glu
5:131672103:T:A	missense	ENST00000510461.6:c.2341A>T	ENSP00000421985.1:p.Thr781 Ser
5:131672106:G:A	missense	ENST00000510461.6:c.2338C>T	ENSP00000421985.1:p.His780 Tyr
5:131672111:C:G	missense	ENST00000510461.6:c.2333G>C	ENSP00000421985.1:p.Arg778 Thr
5:131672111:C:T	missense	ENST00000510461.6:c.2333G>A	ENSP00000421985.1:p.Arg778 Lys
5:131672112:T:C	missense	ENST00000510461.6:c.2332A>G	ENSP00000421985.1:p.Arg778 Gly
5:131672116:A:C	missense	ENST00000510461.6:c.2328T>G	ENSP00000421985.1:p.Ile776 Met
5:131672118:T:A	missense	ENST00000510461.6:c.2326A>T	ENSP00000421985.1:p.Ile776P he
5:131672120:T:C	missense	ENST00000510461.6:c.2324A>G	ENSP00000421985.1:p.Gln775 Arg
5:131672121:G:C	missense	ENST00000510461.6:c.2323C>G	ENSP00000421985.1:p.Gln775 Glu

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5:131672126:A:G	missense	ENST00000510461.6:c.2318T>C	ENSP00000421985.1:p.Val773 Ala
5:131672127:C:T	missense	ENST00000510461.6:c.2317G>A	ENSP00000421985.1:p.Val773 Met
5:131672130:C:T	missense	ENST00000510461.6:c.2314G>A	ENSP00000421985.1:p.Val772 Met
5:131672132:G:A	missense	ENST00000510461.6:c.2312C>T	ENSP00000421985.1:p.Ala771 Val
5:131672132:G:T	missense	ENST00000510461.6:c.2312C>A	ENSP00000421985.1:p.Ala771 Glu
5:131672133:C:T	missense	ENST00000510461.6:c.2311G>A	ENSP00000421985.1:p.Ala771 Thr
5:131672135:T:A	missense	ENST00000510461.6:c.2309A>T	ENSP00000421985.1:p.Gln770 Leu
5:131672136:G:C	missense	ENST00000510461.6:c.2308C>G	ENSP00000421985.1:p.Gln770 Glu
5:131672141:C:G	missense	ENST00000510461.6:c.2303G>C	ENSP00000421985.1:p.Arg768 Pro
5:131672141:C:T	missense	ENST00000510461.6:c.2303G>A	ENSP00000421985.1:p.Arg768 Gln
5:131672142:G:A	stop_gain ed	ENST00000510461.6:c.2302C>T	ENSP00000421985.1:p.Arg768 Ter
5:131672145:G:C	missense	ENST00000510461.6:c.2299C>G	ENSP00000421985.1:p.Leu767 Val
5:131672146:C:G	missense	ENST00000510461.6:c.2298G>C	ENSP00000421985.1:p.Glu766 Asp
5:131672153:T:A	missense	ENST00000510461.6:c.2291A>T	ENSP00000421985.1:p.Asp764 Val
5:131672156:G:C	stop_gain ed	ENST00000510461.6:c.2288C>G	ENSP00000421985.1:p.Ser763 Ter
5:131672157:A:C	missense	ENST00000510461.6:c.2287T>G	ENSP00000421985.1:p.Ser763 Ala
5:131672158:A:C	missense	ENST00000510461.6:c.2286T>G	ENSP00000421985.1:p.Asp762 Glu

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5:131672160:C:T	missense	ENST00000510461.6:c.2284G>A	ENSP00000421985.1:p.Asp762 Asn
5:131672162:G:A	missense	ENST00000510461.6:c.2282C>T	ENSP00000421985.1:p.Pro761 Leu
5:131672163:G:A	missense	ENST00000510461.6:c.2281C>T	ENSP00000421985.1:p.Pro761 Ser
5:131672163:G:C	missense	ENST00000510461.6:c.2281C>G	ENSP00000421985.1:p.Pro761 Ala
5:131672169:T:C	missense	ENST00000510461.6:c.2275A>G	ENSP00000421985.1:p.Met75 9Val
5:131672171:G:A	missense	ENST00000510461.6:c.2273C>T	ENSP00000421985.1:p.Ser758 Phe
5:131672171:G:C	missense	ENST00000510461.6:c.2273C>G	ENSP00000421985.1:p.Ser758 Cys
5:131672172:A:C	missense	ENST00000510461.6:c.2272T>G	ENSP00000421985.1:p.Ser758 Ala
5:131672172:A:G	missense	ENST00000510461.6:c.2272T>C	ENSP00000421985.1:p.Ser758 Pro
5:131672172:A:T	missense	ENST00000510461.6:c.2272T>A	ENSP00000421985.1:p.Ser758 Thr
5:131672174:T:A	missense	ENST00000510461.6:c.2270A>T	ENSP00000421985.1:p.Asp757 Val
5:131672179:A:C	missense	ENST00000510461.6:c.2265T>G	ENSP00000421985.1:p.Ile755 Met
5:131672180:A:G	missense	ENST00000510461.6:c.2264T>C	ENSP00000421985.1:p.Ile755T hr
5:131672181:T:A	missense	ENST00000510461.6:c.2263A>T	ENSP00000421985.1:p.Ile755P he
5:131672189:G:C	missense	ENST00000510461.6:c.2255C>G	ENSP00000421985.1:p.Thr752 Ser
5:131672192:A:G	missense	ENST00000510461.6:c.2252T>C	ENSP00000421985.1:p.Val751 Ala
5:131672193:C:T	missense	ENST00000510461.6:c.2251G>A	ENSP00000421985.1:p.Val751I le

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5:131672195:T:C	missense	ENST00000510461.6:c.2249A>G	ENSP00000421985.1:p.Lys750 Arg
5:131672201:T:C	missense	ENST00000510461.6:c.2243A>G	ENSP00000421985.1:p.Gln748 Arg
5:131672212:A:C	missense	ENST00000510461.6:c.2232T>G	ENSP00000421985.1:p.Cys744 Trp
5:131672213:C:T	missense	ENST00000510461.6:c.2231G>A	ENSP00000421985.1:p.Cys744 Tyr
5:131672233:A:C	missense	ENST00000510461.6:c.2211T>G	ENSP00000421985.1:p.Ile737 Met
5:131672234:A:G	missense	ENST00000510461.6:c.2210T>C	ENSP00000421985.1:p.Ile737T hr
5:131672238:T:C	missense	ENST00000510461.6:c.2206A>G	ENSP00000421985.1:p.Lys736 Glu
5:131672240:T:C	missense	ENST00000510461.6:c.2204A>G	ENSP00000421985.1:p.Asp735 Gly
5:131672240:T:G	missense	ENST00000510461.6:c.2204A>C	ENSP00000421985.1:p.Asp735 Ala
5:131672244:G:A	missense	ENST00000510461.6:c.2200C>T	ENSP00000421985.1:p.Pro734 Ser
5:131672246:G:A	missense	ENST00000510461.6:c.2198C>T	ENSP00000421985.1:p.Pro733 Leu
5:131672247:G:G T	frameshift	ENST00000510461.6:c.2196dup	ENSP00000421985.1:p.Pro733 ThrfsTer4
5:131672247:G:T	missense	ENST00000510461.6:c.2197C>A	ENSP00000421985.1:p.Pro733 Thr
5:131672248:T:G	missense	ENST00000510461.6:c.2196A>C	ENSP00000421985.1:p.Lys732 Asn
5:131672249:T:A	missense	ENST00000510461.6:c.2195A>T	ENSP00000421985.1:p.Lys732I le
5:131672252:T:C	missense	ENST00000510461.6:c.2192A>G	ENSP00000421985.1:p.Lys731 Arg
5:131672253:T:C	missense	ENST00000510461.6:c.2191A>G	ENSP00000421985.1:p.Lys731 Glu

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5:131672254:T:G	missense	ENST00000510461.6:c.2190A>C	ENSP00000421985.1:p.Glu730 Asp
5:131672255:T:C	missense	ENST00000510461.6:c.2189A>G	ENSP00000421985.1:p.Glu730 Gly
5:131672256:C:G	missense	ENST00000510461.6:c.2188G>C	ENSP00000421985.1:p.Glu730 Gln
5:131672256:C:T	missense	ENST00000510461.6:c.2188G>A	ENSP00000421985.1:p.Glu730 Lys
5:131672259:C:G	missense	ENST00000510461.6:c.2185G>C	ENSP00000421985.1:p.Val729 Leu
5:131672261:A:G	missense	ENST00000510461.6:c.2183T>C	ENSP00000421985.1:p.Val728 Ala
5:131672262:C:T	missense	ENST00000510461.6:c.2182G>A	ENSP00000421985.1:p.Val728 Ile
5:131672264:A:G	missense	ENST00000510461.6:c.2180T>C	ENSP00000421985.1:p.Met72 7Thr
5:131672265:T:C	missense	ENST00000510461.6:c.2179A>G	ENSP00000421985.1:p.Met72 7Val
5:131672267:C:A	missense	ENST00000510461.6:c.2177G>T	ENSP00000421985.1:p.Gly726 Val
5:131672268:C:T	missense	ENST00000510461.6:c.2176G>A	ENSP00000421985.1:p.Gly726 Arg
5:131672270:G:A	missense	ENST00000510461.6:c.2174C>T	ENSP00000421985.1:p.Thr725 Ile
5:131672271:T:C	missense	ENST00000510461.6:c.2173A>G	ENSP00000421985.1:p.Thr725 Ala
5:131672271:T:G	missense	ENST00000510461.6:c.2173A>C	ENSP00000421985.1:p.Thr725 Pro
5:131672273:G:A	missense	ENST00000510461.6:c.2171C>T	ENSP00000421985.1:p.Ser724 Phe
5:131672274:A:C	missense	ENST00000510461.6:c.2170T>G	ENSP00000421985.1:p.Ser724 Ala
5:131672274:A:T	missense	ENST00000510461.6:c.2170T>A	ENSP00000421985.1:p.Ser724 Thr

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5:131672278:C:T	missense	ENST00000510461.6:c.2166G>A	ENSP00000421985.1:p.Met722Ile
5:131672279:A:C	missense	ENST00000510461.6:c.2165T>G	ENSP00000421985.1:p.Met722Arg
5:131672280:T:C	missense	ENST00000510461.6:c.2164A>G	ENSP00000421985.1:p.Met722Val
5:131672283:C:T	missense	ENST00000510461.6:c.2161G>A	ENSP00000421985.1:p.Ala721Thr
5:131672285:T:C	missense	ENST00000510461.6:c.2159A>G	ENSP00000421985.1:p.Lys720Arg
5:131672291:G:A	missense	ENST00000510461.6:c.2153C>T	ENSP00000421985.1:p.Thr718Ile
5:131672292:T:G	missense	ENST00000510461.6:c.2152A>C	ENSP00000421985.1:p.Thr718Pro
5:131672296:ACTGT:A	frameshift	ENST00000510461.6:c.2144_2147del	ENSP00000421985.1:p.Asp715ValfsTer7
5:131672303:G:A	missense	ENST00000510461.6:c.2141C>T	ENSP00000421985.1:p.Ser714Leu
5:131672311:C:A	missense	ENST00000510461.6:c.2133G>T	ENSP00000421985.1:p.Leu711Phe
5:131672312:A:G	missense	ENST00000510461.6:c.2132T>C	ENSP00000421985.1:p.Leu711Ser
5:131672320:A:C	missense	ENST00000510461.6:c.2124T>G	ENSP00000421985.1:p.Ser708Arg
5:131672321:C:A	missense	ENST00000510461.6:c.2123G>T	ENSP00000421985.1:p.Ser708Ile
5:131672321:C:T	missense	ENST00000510461.6:c.2123G>A	ENSP00000421985.1:p.Ser708Asn
5:131672324:T:C	missense	ENST00000510461.6:c.2120A>G	ENSP00000421985.1:p.Gln707Arg
5:131672328:A:G	missense	ENST00000510461.6:c.2116T>C	ENSP00000421985.1:p.Trp706Arg
5:131672328:A:T	missense	ENST00000510461.6:c.2116T>A	ENSP00000421985.1:p.Trp706Arg

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5:131672342:G:A	missense	ENST00000510461.6:c.2102C>T	ENSP00000421985.1:p.Ser701 Leu
5:131672343:A:C	missense	ENST00000510461.6:c.2101T>G	ENSP00000421985.1:p.Ser701 Ala
5:131672345:T:C	missense	ENST00000510461.6:c.2099A>G	ENSP00000421985.1:p.Glu700 Gly
5:131672346:C:G	missense	ENST00000510461.6:c.2098G>C	ENSP00000421985.1:p.Glu700 Gln
5:131672346:C:T	missense	ENST00000510461.6:c.2098G>A	ENSP00000421985.1:p.Glu700 Lys
5:131672351:C:T	missense	ENST00000510461.6:c.2093G>A	ENSP00000421985.1:p.Gly698 Asp
5:131672352:C:T	missense	ENST00000510461.6:c.2092G>A	ENSP00000421985.1:p.Gly698 Ser
5:131672357:T:G	missense	ENST00000510461.6:c.2087A>C	ENSP00000421985.1:p.Glu696 Ala
5:131672363:A:C	missense	ENST00000510461.6:c.2081T>G	ENSP00000421985.1:p.Leu694 Trp
5:131672363:A:G	missense	ENST00000510461.6:c.2081T>C	ENSP00000421985.1:p.Leu694 Ser
5:131672367:C:T	missense	ENST00000510461.6:c.2077G>A	ENSP00000421985.1:p.Ala693 Thr
5:131672369:C:T	missense	ENST00000510461.6:c.2075G>A	ENSP00000421985.1:p.Cys692 Tyr
5:131672370:A:G	missense	ENST00000510461.6:c.2074T>C	ENSP00000421985.1:p.Cys692 Arg
5:131672372:T:A	missense	ENST00000510461.6:c.2072A>T	ENSP00000421985.1:p.Lys691I Ile
5:131672375:T:C	missense	ENST00000510461.6:c.2069A>G	ENSP00000421985.1:p.Asp690 Gly
5:131672376:C:T	missense	ENST00000510461.6:c.2068G>A	ENSP00000421985.1:p.Asp690 Asn
5:131672381:G:C	missense	ENST00000510461.6:c.2063C>G	ENSP00000421985.1:p.Pro688 Arg

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5:131672382:G:C	missense	ENST00000510461.6:c.2062C>G	ENSP00000421985.1:p.Pro688 Ala
5:131672382:G:T	missense	ENST00000510461.6:c.2062C>A	ENSP00000421985.1:p.Pro688 Thr
5:131672385:C:T	missense	ENST00000510461.6:c.2059G>A	ENSP00000421985.1:p.Val687I le
5:131672387:G:C	missense	ENST00000510461.6:c.2057C>G	ENSP00000421985.1:p.Ser686 Cys
5:131672389:TC: T	frameshif t	ENST00000510461.6:c.2054del	ENSP00000421985.1:p.Gly685 AspfsTer5
5:131672390:C:T	missense	ENST00000510461.6:c.2054G>A	ENSP00000421985.1:p.Gly685 Glu
5:131672391:C:T	missense	ENST00000510461.6:c.2053G>A	ENSP00000421985.1:p.Gly685 Arg
5:131672393:G:A	missense	ENST00000510461.6:c.2051C>T	ENSP00000421985.1:p.Thr684 Ile
5:131672394:T:G	missense	ENST00000510461.6:c.2050A>C	ENSP00000421985.1:p.Thr684 Pro
5:131672396:CA: C	frameshif t	ENST00000510461.6:c.2047del	ENSP00000421985.1:p.Cys683 AlafsTer7
5:131672400:C:A	missense	ENST00000510461.6:c.2044G>T	ENSP00000421985.1:p.Val682 Phe
5:131672405:G:A	missense	ENST00000510461.6:c.2039C>T	ENSP00000421985.1:p.Thr680 Ile
5:131672406:T:C	missense	ENST00000510461.6:c.2038A>G	ENSP00000421985.1:p.Thr680 Ala
5:131672408:T:C	missense	ENST00000510461.6:c.2036A>G	ENSP00000421985.1:p.Glu679 Gly
5:131672409:C:G	missense	ENST00000510461.6:c.2035G>C	ENSP00000421985.1:p.Glu679 Gln
5:131672417:G:T	missense	ENST00000510461.6:c.2027C>A	ENSP00000421985.1:p.Ala676 Asp
5:131672418:C:A	missense	ENST00000510461.6:c.2026G>T	ENSP00000421985.1:p.Ala676 Ser

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5:131672418:C:T	missense	ENST00000510461.6:c.2026G>A	ENSP00000421985.1:p.Ala676 Thr
5:131672420:T:C	missense	ENST00000510461.6:c.2024A>G	ENSP00000421985.1:p.Asp675 Gly
5:131672423:A:G	missense	ENST00000510461.6:c.2021T>C	ENSP00000421985.1:p.Phe67 4Ser
5:131672424:A:G	missense	ENST00000510461.6:c.2020T>C	ENSP00000421985.1:p.Phe67 4Leu
5:131672424:AG: A	frameshif t	ENST00000510461.6:c.2019del	ENSP00000421985.1:p.Phe67 4LeufsTer5
5:131672427:A:C	missense	ENST00000510461.6:c.2017T>G	ENSP00000421985.1:p.Cys673 Gly
5:131672430:T:A	missense	ENST00000510461.6:c.2014A>T	ENSP00000421985.1:p.Thr672 Ser
5:131672430:T:C	missense	ENST00000510461.6:c.2014A>G	ENSP00000421985.1:p.Thr672 Ala
5:131672436:A:T	missense	ENST00000510461.6:c.2008T>A	ENSP00000421985.1:p.Leu670 Ile
5:131672438:T:G	missense	ENST00000510461.6:c.2006A>C	ENSP00000421985.1:p.Lys669 Thr
5:131672439:T:C	missense	ENST00000510461.6:c.2005A>G	ENSP00000421985.1:p.Lys669 Glu
5:131672440:A:T	missense	ENST00000510461.6:c.2004T>A	ENSP00000421985.1:p.Asp668 Glu
5:131672441:T:C	missense	ENST00000510461.6:c.2003A>G	ENSP00000421985.1:p.Asp668 Gly
5:131672442:C:T	missense	ENST00000510461.6:c.2002G>A	ENSP00000421985.1:p.Asp668 Asn
5:131672444:C:G	missense	ENST00000510461.6:c.2000G>C	ENSP00000421985.1:p.Arg667 Thr
5:131672447:T:C	missense	ENST00000510461.6:c.1997A>G	ENSP00000421985.1:p.Tyr666 Cys
5:131672448:A:G	missense	ENST00000510461.6:c.1996T>C	ENSP00000421985.1:p.Tyr666 His

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5:131672449:C:G	missense	ENST00000510461.6:c.1995G>C	ENSP00000421985.1:p.Gln665 His
5:131672450:T:C	missense	ENST00000510461.6:c.1994A>G	ENSP00000421985.1:p.Gln665 Arg
5:131672454:T:C	missense	ENST00000510461.6:c.1990A>G	ENSP00000421985.1:p.Lys664 Glu
5:131672457:C:T	missense	ENST00000510461.6:c.1987G>A	ENSP00000421985.1:p.Val663I le
5:131672457:CA: C	frameshif t	ENST00000510461.6:c.1986del	ENSP00000421985.1:p.Asp662 GlufsTer9
5:131672460:C:T	missense	ENST00000510461.6:c.1984G>A	ENSP00000421985.1:p.Asp662 Asn
5:131672463:C:T	missense	ENST00000510461.6:c.1981G>A	ENSP00000421985.1:p.Val661I le
5:131672465:G:T	missense	ENST00000510461.6:c.1979C>A	ENSP00000421985.1:p.Ala660 Asp
5:131672466:C:T	missense	ENST00000510461.6:c.1978G>A	ENSP00000421985.1:p.Ala660 Thr
5:131672468:T:C	missense	ENST00000510461.6:c.1976A>G	ENSP00000421985.1:p.Asn659 Ser
5:131672471:T:C	missense	ENST00000510461.6:c.1973A>G	ENSP00000421985.1:p.Glu658 Gly
5:131672474:T:C	missense	ENST00000510461.6:c.1970A>G	ENSP00000421985.1:p.Glu657 Gly
5:131672475:C:T	missense	ENST00000510461.6:c.1969G>A	ENSP00000421985.1:p.Glu657 Lys
5:131672477:T:A	missense	ENST00000510461.6:c.1967A>T	ENSP00000421985.1:p.Gln656 Leu
5:131672478:G:A	stop_gain ed	ENST00000510461.6:c.1966C>T	ENSP00000421985.1:p.Gln656 Ter
5:131672482:G:C	missense	ENST00000510461.6:c.1962C>G	ENSP00000421985.1:p.Asp654 Glu
5:131672486:G:A	missense	ENST00000510461.6:c.1958C>T	ENSP00000421985.1:p.Ser653 Phe

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5:131672490:G:A	missense	ENST00000510461.6:c.1954C>T	ENSP00000421985.1:p.Pro652 Ser
5:131672502:G:A	stop_gained	ENST00000510461.6:c.1942C>T	ENSP00000421985.1:p.Gln648 Ter
5:131672504:C:T	missense	ENST00000510461.6:c.1940G>A	ENSP00000421985.1:p.Cys647 Tyr
5:131672505:A:G	missense	ENST00000510461.6:c.1939T>C	ENSP00000421985.1:p.Cys647 Arg
5:131672507:T:G	missense	ENST00000510461.6:c.1937A>C	ENSP00000421985.1:p.Glu646 Ala
5:131672508:C:G	missense	ENST00000510461.6:c.1936G>C	ENSP00000421985.1:p.Glu646 Gln
5:131672509:A:C	missense	ENST00000510461.6:c.1935T>G	ENSP00000421985.1:p.Asp645 Glu
5:131672511:C:G	missense	ENST00000510461.6:c.1933G>C	ENSP00000421985.1:p.Asp645 His
5:131672517:T:C	missense	ENST00000510461.6:c.1927A>G	ENSP00000421985.1:p.Ile643 Val
5:131672519:C:T	missense	ENST00000510461.6:c.1925G>A	ENSP00000421985.1:p.Gly642 Glu
5:131672522:A:G	missense	ENST00000510461.6:c.1922T>C	ENSP00000421985.1:p.Leu641 Pro
5:131672527:C:G	missense	ENST00000510461.6:c.1917G>C	ENSP00000421985.1:p.Glu639 Asp
5:131672529:C:T	missense	ENST00000510461.6:c.1915G>A	ENSP00000421985.1:p.Glu639 Lys
5:131672534:G:A	missense	ENST00000510461.6:c.1910C>T	ENSP00000421985.1:p.Ser637 Phe
5:131672543:T:G	missense	ENST00000510461.6:c.1901A>C	ENSP00000421985.1:p.Gln634 Pro
5:131672552:T:C	missense	ENST00000510461.6:c.1892A>G	ENSP00000421985.1:p.Glu631 Gly
5:131672553:C:A	stop_gained	ENST00000510461.6:c.1891G>T	ENSP00000421985.1:p.Glu631 Ter

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5:131672553:C:G	missense	ENST00000510461.6:c.1891G>C	ENSP00000421985.1:p.Glu631 Gln
5:131672557:C:G	missense	ENST00000510461.6:c.1887G>C	ENSP00000421985.1:p.Glu629 Asp
5:131672559:C:G	missense	ENST00000510461.6:c.1885G>C	ENSP00000421985.1:p.Glu629 Gln
5:131672559:CTT :C	frameshift	ENST00000510461.6:c.1883_18 84del	ENSP00000421985.1:p.Gln628 ArgfsTer10
5:131672562:G:C	missense	ENST00000510461.6:c.1882C>G	ENSP00000421985.1:p.Gln628 Glu
5:131672562:G:T	missense	ENST00000510461.6:c.1882C>A	ENSP00000421985.1:p.Gln628 Lys
5:131672567:G:A	missense	ENST00000510461.6:c.1877C>T	ENSP00000421985.1:p.Ser626 Leu
5:131672568:A:T	missense	ENST00000510461.6:c.1876T>A	ENSP00000421985.1:p.Ser626 Thr
5:131672575:C:A	missense	ENST00000510461.6:c.1869G>T	ENSP00000421985.1:p.Glu623 Asp
5:131672582:T:G	missense	ENST00000510461.6:c.1862A>C	ENSP00000421985.1:p.Asn621 Thr
5:131672583:T:G	missense	ENST00000510461.6:c.1861A>C	ENSP00000421985.1:p.Asn621 His
5:131672588:C:G	missense	ENST00000510461.6:c.1856G>C	ENSP00000421985.1:p.Gly619 Ala
5:131672594:A:G	missense	ENST00000510461.6:c.1850T>C	ENSP00000421985.1:p.Leu617 Pro
5:131672595:G:A	missense	ENST00000510461.6:c.1849C>T	ENSP00000421985.1:p.Leu617 Phe
5:131672595:G:C	missense	ENST00000510461.6:c.1849C>G	ENSP00000421985.1:p.Leu617 Val
5:131672597:G:A	missense	ENST00000510461.6:c.1847C>T	ENSP00000421985.1:p.Pro616 Leu
5:131672598:G:A	missense	ENST00000510461.6:c.1846C>T	ENSP00000421985.1:p.Pro616 Ser

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5:131672602:A:T	missense	ENST00000510461.6:c.1842T>A	ENSP00000421985.1:p.Ser614 Arg
5:131672603:C:T	missense	ENST00000510461.6:c.1841G>A	ENSP00000421985.1:p.Ser614 Asn
5:131672606:C:T	missense	ENST00000510461.6:c.1838G>A	ENSP00000421985.1:p.Cys613 Tyr
5:131672610:A:G	missense	ENST00000510461.6:c.1834T>C	ENSP00000421985.1:p.Tyr612 His
5:131672613:TAC :T	frameshift	ENST00000510461.6:c.1829_18 30del	ENSP00000421985.1:p.Cys610 Ter
5:131672621:C:A	missense	ENST00000510461.6:c.1823G>T	ENSP00000421985.1:p.Cys608 Phe
5:131672621:C:G	missense	ENST00000510461.6:c.1823G>C	ENSP00000421985.1:p.Cys608 Ser
5:131672621:C:T	missense	ENST00000510461.6:c.1823G>A	ENSP00000421985.1:p.Cys608 Tyr
5:131672622:A:T	missense	ENST00000510461.6:c.1822T>A	ENSP00000421985.1:p.Cys608 Ser
5:131672627:G:A	missense	ENST00000510461.6:c.1817C>T	ENSP00000421985.1:p.Pro606 Leu
5:131672632:TC: T	frameshift	ENST00000510461.6:c.1811del	ENSP00000421985.1:p.Arg604 LysfsTer19
5:131672633:C:G	missense	ENST00000510461.6:c.1811G>C	ENSP00000421985.1:p.Arg604 Thr
5:131672648:T:C	missense	ENST00000510461.6:c.1796A>G	ENSP00000421985.1:p.Glu599 Gly
5:131672649:C:G	missense	ENST00000510461.6:c.1795G>C	ENSP00000421985.1:p.Glu599 Gln
5:131672651:T:C	missense	ENST00000510461.6:c.1793A>G	ENSP00000421985.1:p.Lys598 Arg
5:131672651:T:G	missense	ENST00000510461.6:c.1793A>C	ENSP00000421985.1:p.Lys598 Thr
5:131672652:T:C	missense	ENST00000510461.6:c.1792A>G	ENSP00000421985.1:p.Lys598 Glu

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5:131672654:A:G	missense	ENST00000510461.6:c.1790T>C	ENSP00000421985.1:p.Phe597Ser
5:131672655:A:G	missense	ENST00000510461.6:c.1789T>C	ENSP00000421985.1:p.Phe597Leu
5:131672658:G:A	missense	ENST00000510461.6:c.1786C>T	ENSP00000421985.1:p.Leu596Phe
5:131672662:A:C	missense	ENST00000510461.6:c.1782T>G	ENSP00000421985.1:p.Ser594Arg
5:131672664:T:A	missense	ENST00000510461.6:c.1780A>T	ENSP00000421985.1:p.Ser594Cys
5:131672664:T:C	missense	ENST00000510461.6:c.1780A>G	ENSP00000421985.1:p.Ser594Gly
5:131672665:G:C	missense	ENST00000510461.6:c.1779C>G	ENSP00000421985.1:p.Ser593Arg
5:131672669:T:C	missense	ENST00000510461.6:c.1775A>G	ENSP00000421985.1:p.Lys592Arg
5:131672678:T:C	missense	ENST00000510461.6:c.1766A>G	ENSP00000421985.1:p.His589Arg
5:131672682:T:C	missense	ENST00000510461.6:c.1762A>G	ENSP00000421985.1:p.Met588Val
5:131672684:G:T	missense	ENST00000510461.6:c.1760C>A	ENSP00000421985.1:p.Thr587Lys
5:131672688:C:G	missense	ENST00000510461.6:c.1756G>C	ENSP00000421985.1:p.Val586Leu
5:131672688:C:T	missense	ENST00000510461.6:c.1756G>A	ENSP00000421985.1:p.Val586Ile
5:131672695:A:T	stop_gained	ENST00000510461.6:c.1749T>A	ENSP00000421985.1:p.Tyr583Ter
5:131672696:TAC TCTGATTC:T	frameshift	ENST00000510461.6:c.1738_1747del	ENSP00000421985.1:p.Glu580MetfsTer40
5:131672699:T:A	missense	ENST00000510461.6:c.1745A>T	ENSP00000421985.1:p.Glu582Val
5:131672699:T:G	missense	ENST00000510461.6:c.1745A>C	ENSP00000421985.1:p.Glu582Ala

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5:131672700:C:G	missense	ENST00000510461.6:c.1744G>C	ENSP00000421985.1:p.Glu582 Gln
5:131672710:T:C	missense	ENST00000510461.6:c.1734A>G	ENSP00000421985.1:p.Ile578 Met
5:131672711:A:T	missense	ENST00000510461.6:c.1733T>A	ENSP00000421985.1:p.Ile578L ys
5:131672712:T:C	missense	ENST00000510461.6:c.1732A>G	ENSP00000421985.1:p.Ile578 Val
5:131672714:T:C	missense	ENST00000510461.6:c.1730A>G	ENSP00000421985.1:p.Glu577 Gly
5:131672717:C:T	missense	ENST00000510461.6:c.1727G>A	ENSP00000421985.1:p.Gly576 Asp
5:131672720:TTC :T	frameshift	ENST00000510461.6:c.1722_17 23del	ENSP00000421985.1:p.Lys575 ArgfsTer2
5:131672725:T:G	missense	ENST00000510461.6:c.1719A>C	ENSP00000421985.1:p.Leu573 Phe
5:131672729:G:A	missense	ENST00000510461.6:c.1715C>T	ENSP00000421985.1:p.Thr572 Ile
5:131672730:T:C	missense	ENST00000510461.6:c.1714A>G	ENSP00000421985.1:p.Thr572 Ala
5:131672730:T:G	missense	ENST00000510461.6:c.1714A>C	ENSP00000421985.1:p.Thr572 Pro
5:131672732:G:A	missense	ENST00000510461.6:c.1712C>T	ENSP00000421985.1:p.Thr571 Ile
5:131672732:G:T	missense	ENST00000510461.6:c.1712C>A	ENSP00000421985.1:p.Thr571 Asn
5:131672733:T:C	missense	ENST00000510461.6:c.1711A>G	ENSP00000421985.1:p.Thr571 Ala
5:131672738:A:G	missense	ENST00000510461.6:c.1706T>C	ENSP00000421985.1:p.Ile569T hr
5:131672742:C:A	missense	ENST00000510461.6:c.1702G>T	ENSP00000421985.1:p.Val568 Leu
5:131672744:G:C	missense	ENST00000510461.6:c.1700C>G	ENSP00000421985.1:p.Thr567 Arg

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5:131672747:C:T	missense	ENST00000510461.6:c.1697G>A	ENSP00000421985.1:p.Gly566 Asp
5:131672748:C:G	missense	ENST00000510461.6:c.1696G>C	ENSP00000421985.1:p.Gly566 Arg
5:131672751:G:A	missense	ENST00000510461.6:c.1693C>T	ENSP00000421985.1:p.Pro565 Ser
5:131672753:A:G	missense	ENST00000510461.6:c.1691T>C	ENSP00000421985.1:p.Met56 4Thr
5:131672757:C:T	missense	ENST00000510461.6:c.1687G>A	ENSP00000421985.1:p.Val563I le
5:131672758:G:C	missense	ENST00000510461.6:c.1686C>G	ENSP00000421985.1:p.Ile562 Met
5:131672762:G:A	missense	ENST00000510461.6:c.1682C>T	ENSP00000421985.1:p.Ala561 Val
5:131672767:A:C	missense	ENST00000510461.6:c.1677T>G	ENSP00000421985.1:p.Asp559 Glu
5:131672767:A:T	missense	ENST00000510461.6:c.1677T>A	ENSP00000421985.1:p.Asp559 Glu
5:131672768:T:C	missense	ENST00000510461.6:c.1676A>G	ENSP00000421985.1:p.Asp559 Gly
5:131672769:C:T	missense	ENST00000510461.6:c.1675G>A	ENSP00000421985.1:p.Asp559 Asn
5:131672770:T:G	missense	ENST00000510461.6:c.1674A>C	ENSP00000421985.1:p.Glu558 Asp
5:131672771:T:A	missense	ENST00000510461.6:c.1673A>T	ENSP00000421985.1:p.Glu558 Val
5:131672783:A:G	missense	ENST00000510461.6:c.1661T>C	ENSP00000421985.1:p.Leu554 Ser
5:131672784:A:C	missense	ENST00000510461.6:c.1660T>G	ENSP00000421985.1:p.Leu554 Val
5:131672787:G:C	missense	ENST00000510461.6:c.1657C>G	ENSP00000421985.1:p.Leu553 Val
5:131672792:G:A	missense	ENST00000510461.6:c.1652C>T	ENSP00000421985.1:p.Thr551 Met

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5:131672793:T:C	missense	ENST00000510461.6:c.1651A>G	ENSP00000421985.1:p.Thr551 Ala
5:131672798:T:G	missense	ENST00000510461.6:c.1646A>C	ENSP00000421985.1:p.Gln549 Pro
5:131672799:G:T	missense	ENST00000510461.6:c.1645C>A	ENSP00000421985.1:p.Gln549 Lys
5:131672801:A:G	missense	ENST00000510461.6:c.1643T>C	ENSP00000421985.1:p.Leu548 Pro
5:131672802:G:A	missense	ENST00000510461.6:c.1642C>T	ENSP00000421985.1:p.Leu548 Phe
5:131672816:A:G	missense	ENST00000510461.6:c.1628T>C	ENSP00000421985.1:p.Ile543T hr
5:131672817:T:A	missense	ENST00000510461.6:c.1627A>T	ENSP00000421985.1:p.Ile543L eu
5:131672825:G:C	missense	ENST00000510461.6:c.1619C>G	ENSP00000421985.1:p.Thr540 Ser
5:131672826:T:A	missense	ENST00000510461.6:c.1618A>T	ENSP00000421985.1:p.Thr540 Ser
5:131672833:ATA AAG:A	frameshift	ENST00000510461.6:c.1606_16 10del	ENSP00000421985.1:p.Leu536 PhefsTer10
5:131672834:T:C	missense	ENST00000510461.6:c.1610A>G	ENSP00000421985.1:p.Tyr537 Cys
5:131672837:A:T	missense	ENST00000510461.6:c.1607T>A	ENSP00000421985.1:p.Leu536 His
5:131672841:G:C	missense	ENST00000510461.6:c.1603C>G	ENSP00000421985.1:p.Leu535 Val
5:131672843:C:A	missense	ENST00000510461.6:c.1601G>T	ENSP00000421985.1:p.Arg534 Met
5:131672843:C:T	missense	ENST00000510461.6:c.1601G>A	ENSP00000421985.1:p.Arg534 Lys
5:131672847:G:C	missense	ENST00000510461.6:c.1597C>G	ENSP00000421985.1:p.Gln533 Glu
5:131672850:C:T	missense	ENST00000510461.6:c.1594G>A	ENSP00000421985.1:p.Val532I le

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5:131672853:T:C	missense	ENST00000510461.6:c.1591A>G	ENSP00000421985.1:p.Met531Val
5:131672856:C:A	missense	ENST00000510461.6:c.1588G>T	ENSP00000421985.1:p.Asp530Tyr
5:131672856:C:T	missense	ENST00000510461.6:c.1588G>A	ENSP00000421985.1:p.Asp530Asn
5:131672857:T:G	missense	ENST00000510461.6:c.1587A>C	ENSP00000421985.1:p.Gln529His
5:131672859:G:C	missense	ENST00000510461.6:c.1585C>G	ENSP00000421985.1:p.Gln529Glu
5:131672859:G:T	missense	ENST00000510461.6:c.1585C>A	ENSP00000421985.1:p.Gln529Lys
5:131672861:C:A	missense	ENST00000510461.6:c.1583G>T	ENSP00000421985.1:p.Arg528Leu
5:131672861:C:T	missense	ENST00000510461.6:c.1583G>A	ENSP00000421985.1:p.Arg528Gln
5:131672862:G:A	stop_gained	ENST00000510461.6:c.1582C>T	ENSP00000421985.1:p.Arg528Ter
5:131672864:T:C	missense	ENST00000510461.6:c.1580A>G	ENSP00000421985.1:p.Lys527Arg
5:131672865:T:C	missense	ENST00000510461.6:c.1579A>G	ENSP00000421985.1:p.Lys527Glu
5:131672870:A:G	missense	ENST00000510461.6:c.1574T>C	ENSP00000421985.1:p.Val525Ala
5:131672873:A:G	missense	ENST00000510461.6:c.1571T>C	ENSP00000421985.1:p.Val524Ala
5:131672876:A:G	missense	ENST00000510461.6:c.1568T>C	ENSP00000421985.1:p.Val523Ala
5:131672877:C:G	missense	ENST00000510461.6:c.1567G>C	ENSP00000421985.1:p.Val523Leu
5:131672879:G:C	missense	ENST00000510461.6:c.1565C>G	ENSP00000421985.1:p.Thr522Ser
5:131672880:T:C	missense	ENST00000510461.6:c.1564A>G	ENSP00000421985.1:p.Thr522Ala

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5:131672886:C:T	missense	ENST00000510461.6:c.1558G>A	ENSP00000421985.1:p.Ala520 Thr
5:131672889:A:T	missense	ENST00000510461.6:c.1555T>A	ENSP00000421985.1:p.Leu519 Ile
5:131672891:C:T	missense	ENST00000510461.6:c.1553G>A	ENSP00000421985.1:p.Arg518 Gln
5:131672892:G:A	missense	ENST00000510461.6:c.1552C>T	ENSP00000421985.1:p.Arg518 Trp
5:131672895:C:A	missense	ENST00000510461.6:c.1549G>T	ENSP00000421985.1:p.Val517 Leu
5:131672895:C:T	missense	ENST00000510461.6:c.1549G>A	ENSP00000421985.1:p.Val517 Ile
5:131672900:G:A	missense	ENST00000510461.6:c.1544C>T	ENSP00000421985.1:p.Ser515 Phe
5:131672901:A:G	missense	ENST00000510461.6:c.1543T>C	ENSP00000421985.1:p.Ser515 Pro
5:131672903:C:A	missense	ENST00000510461.6:c.1541G>T	ENSP00000421985.1:p.Gly514 Val
5:131672903:C:G	missense	ENST00000510461.6:c.1541G>C	ENSP00000421985.1:p.Gly514 Ala
5:131672903:C:T	missense	ENST00000510461.6:c.1541G>A	ENSP00000421985.1:p.Gly514 Asp
5:131672906:A:C	missense	ENST00000510461.6:c.1538T>G	ENSP00000421985.1:p.Ile513S Ser
5:131672906:A:G	missense	ENST00000510461.6:c.1538T>C	ENSP00000421985.1:p.Ile513T Thr
5:131672910:C:A	missense	ENST00000510461.6:c.1534G>T	ENSP00000421985.1:p.Ala512 Ser
5:131672910:C:T	missense	ENST00000510461.6:c.1534G>A	ENSP00000421985.1:p.Ala512 Thr
5:131672912:C:G	missense	ENST00000510461.6:c.1532G>C	ENSP00000421985.1:p.Gly511 Ala
5:131672912:C:T	missense	ENST00000510461.6:c.1532G>A	ENSP00000421985.1:p.Gly511 Asp

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5:131672915:T:C	missense	ENST00000510461.6:c.1529A>G	ENSP00000421985.1:p.Tyr510 Cys
5:131672916:A:G	missense	ENST00000510461.6:c.1528T>C	ENSP00000421985.1:p.Tyr510 His
5:131672918:A:G	missense	ENST00000510461.6:c.1526T>C	ENSP00000421985.1:p.Leu509 Ser
5:131672920:G:C	missense	ENST00000510461.6:c.1524C>G	ENSP00000421985.1:p.Asp508 Glu
5:131677702:C:G	splice_donor	ENST00000510461.6:c.1519+1G>C	NA
5:131677703:C:T	missense	ENST00000510461.6:c.1519G>A	ENSP00000421985.1:p.Gly507 Arg
5:131677713:C:T	stop_gained	ENST00000510461.6:c.1509G>A	ENSP00000421985.1:p.Trp503 Ter
5:131677721:G:A	missense	ENST00000510461.6:c.1501C>T	ENSP00000421985.1:p.Pro501 Ser
5:131677723:T:C	missense	ENST00000510461.6:c.1499A>G	ENSP00000421985.1:p.Asn500 Ser
5:131677736:T:C	missense	ENST00000510461.6:c.1486A>G	ENSP00000421985.1:p.Thr496 Ala
5:131677738:T:C	missense	ENST00000510461.6:c.1484A>G	ENSP00000421985.1:p.Lys495 Arg
5:131677738:T:G	missense	ENST00000510461.6:c.1484A>C	ENSP00000421985.1:p.Lys495 Thr
5:131677742:C:A	missense	ENST00000510461.6:c.1480G>T	ENSP00000421985.1:p.Ala494 Ser
5:131677748:T:C	missense	ENST00000510461.6:c.1474A>G	ENSP00000421985.1:p.Met49 2Val
5:131677751:C:T	missense	ENST00000510461.6:c.1471G>A	ENSP00000421985.1:p.Asp491 Asn
5:131677755:A:C	missense	ENST00000510461.6:c.1467T>G	ENSP00000421985.1:p.Ser489 Arg
5:131677756:C:T	missense	ENST00000510461.6:c.1466G>A	ENSP00000421985.1:p.Ser489 Asn

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5:131677759:T:C	missense	ENST00000510461.6:c.1463A>G	ENSP00000421985.1:p.Gln488 Arg
5:131677768:T:A	missense	ENST00000510461.6:c.1454A>T	ENSP00000421985.1:p.His485 Leu
5:131677780:A:C	missense	ENST00000510461.6:c.1442T>G	ENSP00000421985.1:p.Phe48 1Cys
5:131677780:A:G	missense	ENST00000510461.6:c.1442T>C	ENSP00000421985.1:p.Phe48 1Ser
5:131677781:A:C	missense	ENST00000510461.6:c.1441T>G	ENSP00000421985.1:p.Phe48 1Val
5:131677782:T:C	missense	ENST00000510461.6:c.1440A>G	ENSP00000421985.1:p.Ile480 Met
5:131677783:A:G	missense	ENST00000510461.6:c.1439T>C	ENSP00000421985.1:p.Ile480T hr
5:131677790:T:C	missense	ENST00000510461.6:c.1432A>G	ENSP00000421985.1:p.Ile478 Val
5:131677790:T:G	missense	ENST00000510461.6:c.1432A>C	ENSP00000421985.1:p.Ile478L eu
5:131677792:G:C	missense	ENST00000510461.6:c.1430C>G	ENSP00000421985.1:p.Pro477 Arg
5:131677793:G:A	missense	ENST00000510461.6:c.1429C>T	ENSP00000421985.1:p.Pro477 Ser
5:131677796:G:C	missense	ENST00000510461.6:c.1426C>G	ENSP00000421985.1:p.Pro476 Ala
5:131677804:T:C	missense	ENST00000510461.6:c.1418A>G	ENSP00000421985.1:p.Asn473 Ser
5:131677807:G:A	missense	ENST00000510461.6:c.1415C>T	ENSP00000421985.1:p.Pro472 Leu
5:131677811:T:C	missense	ENST00000510461.6:c.1411A>G	ENSP00000421985.1:p.Met47 1Val
5:131677811:T:G	missense	ENST00000510461.6:c.1411A>C	ENSP00000421985.1:p.Met47 1Leu
5:131677819:G:A	missense	ENST00000510461.6:c.1403C>T	ENSP00000421985.1:p.Pro468 Leu

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5:131677823:C:T	missense	ENST00000510461.6:c.1399G>A	ENSP00000421985.1:p.Val467Ile
5:131677829:C:T	missense	ENST00000510461.6:c.1393G>A	ENSP00000421985.1:p.Ala465Thr
5:131677835:G:A	missense	ENST00000510461.6:c.1387C>T	ENSP00000421985.1:p.His463Tyr
5:131677837:T:C	missense	ENST00000510461.6:c.1385A>G	ENSP00000421985.1:p.Asn462Ser
5:131677838:T:A	missense	ENST00000510461.6:c.1384A>T	ENSP00000421985.1:p.Asn462Tyr
5:131677840:G:A	missense	ENST00000510461.6:c.1382C>T	ENSP00000421985.1:p.Thr461Ile
5:131677840:G:C	missense	ENST00000510461.6:c.1382C>G	ENSP00000421985.1:p.Thr461Ser
5:131677847:C:G	missense	ENST00000510461.6:c.1375G>C	ENSP00000421985.1:p.Val459Leu
5:131677849:G:A	missense	ENST00000510461.6:c.1373C>T	ENSP00000421985.1:p.Ala458Val
5:131677856:T:C	missense	ENST00000510461.6:c.1366A>G	ENSP00000421985.1:p.Ile456Val
5:131677856:T:G	missense	ENST00000510461.6:c.1366A>C	ENSP00000421985.1:p.Ile456Leu
5:131677859:G:A	missense	ENST00000510461.6:c.1363C>T	ENSP00000421985.1:p.Leu455Phe
5:131677859:G:C	missense	ENST00000510461.6:c.1363C>G	ENSP00000421985.1:p.Leu455Val
5:131677865:G:A	missense	ENST00000510461.6:c.1357C>T	ENSP00000421985.1:p.Pro453Ser
5:131677869:G:C	missense	ENST00000510461.6:c.1353C>G	ENSP00000421985.1:p.Phe451Leu
5:131679030:G:T	missense	ENST00000510461.6:c.1348C>A	ENSP00000421985.1:p.Gln450Lys
5:131679032:T:C	missense	ENST00000510461.6:c.1346A>G	ENSP00000421985.1:p.Asn449Ser

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5:131679032:T:G	missense	ENST00000510461.6:c.1346A>C	ENSP00000421985.1:p.Asn449 Thr
5:131679033:T:A	missense	ENST00000510461.6:c.1345A>T	ENSP00000421985.1:p.Asn449 Tyr
5:131679041:G:A	missense	ENST00000510461.6:c.1337C>T	ENSP00000421985.1:p.Ala446 Val
5:131679044:T:C	missense	ENST00000510461.6:c.1334A>G	ENSP00000421985.1:p.Asn445 Ser
5:131679048:C:G	missense	ENST00000510461.6:c.1330G>C	ENSP00000421985.1:p.Glu444 Gln
5:131679050:A:T	missense	ENST00000510461.6:c.1328T>A	ENSP00000421985.1:p.Met44 3Lys
5:131679060:T:C	missense	ENST00000510461.6:c.1318A>G	ENSP00000421985.1:p.Thr440 Ala
5:131679061:G:C	missense	ENST00000510461.6:c.1317C>G	ENSP00000421985.1:p.Phe43 9Leu
5:131679062:A:T	missense	ENST00000510461.6:c.1316T>A	ENSP00000421985.1:p.Phe43 9Tyr
5:131679064:C:A	missense	ENST00000510461.6:c.1314G>T	ENSP00000421985.1:p.Glu438 Asp
5:131679066:C:G	missense	ENST00000510461.6:c.1312G>C	ENSP00000421985.1:p.Glu438 Gln
5:131679066:C:T	missense	ENST00000510461.6:c.1312G>A	ENSP00000421985.1:p.Glu438 Lys
5:131679069:T:C	missense	ENST00000510461.6:c.1309A>G	ENSP00000421985.1:p.Lys437 Glu
5:131679070:C:A	missense	ENST00000510461.6:c.1308G>T	ENSP00000421985.1:p.Met43 6Ile
5:131679072:T:A	missense	ENST00000510461.6:c.1306A>T	ENSP00000421985.1:p.Met43 6Leu
5:131679072:T:C	missense	ENST00000510461.6:c.1306A>G	ENSP00000421985.1:p.Met43 6Val
5:131679073:G:C	missense	ENST00000510461.6:c.1305C>G	ENSP00000421985.1:p.Phe43 5Leu

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5:131679074:A:C	missense	ENST00000510461.6:c.1304T>G	ENSP00000421985.1:p.Phe43 5Cys
5:131679077:C:T	missense	ENST00000510461.6:c.1301G>A	ENSP00000421985.1:p.Arg434 His
5:131679078:G:A	missense	ENST00000510461.6:c.1300C>T	ENSP00000421985.1:p.Arg434 Cys
5:131679078:G:T	missense	ENST00000510461.6:c.1300C>A	ENSP00000421985.1:p.Arg434 Ser
5:131679079:A:T	stop_gain ed	ENST00000510461.6:c.1299T>A	ENSP00000421985.1:p.Tyr433 Ter
5:131679080:T:C	missense	ENST00000510461.6:c.1298A>G	ENSP00000421985.1:p.Tyr433 Cys
5:131679083:C:A	missense	ENST00000510461.6:c.1295G>T	ENSP00000421985.1:p.Cys432 Phe
5:131679084:A:C	missense	ENST00000510461.6:c.1294T>G	ENSP00000421985.1:p.Cys432 Gly
5:131679087:G:A	missense	ENST00000510461.6:c.1291C>T	ENSP00000421985.1:p.Leu431 Phe
5:131679087:G:C	missense	ENST00000510461.6:c.1291C>G	ENSP00000421985.1:p.Leu431 Val
5:131679088:G:T	missense	ENST00000510461.6:c.1290C>A	ENSP00000421985.1:p.His430 Gln
5:131679089:T:C	missense	ENST00000510461.6:c.1289A>G	ENSP00000421985.1:p.His430 Arg
5:131679092:T:C	missense	ENST00000510461.6:c.1286A>G	ENSP00000421985.1:p.Asn429 Ser
5:131679094:C:A	missense	ENST00000510461.6:c.1284G>T	ENSP00000421985.1:p.Lys428 Asn
5:131679102:G:A	missense	ENST00000510461.6:c.1276C>T	ENSP00000421985.1:p.Pro426 Ser
5:131679102:G:T	missense	ENST00000510461.6:c.1276C>A	ENSP00000421985.1:p.Pro426 Thr
5:131679104:G:A	missense	ENST00000510461.6:c.1274C>T	ENSP00000421985.1:p.Thr425 Ile

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5:131679107:C:G	missense	ENST00000510461.6:c.1271G>C	ENSP00000421985.1:p.Gly424 Ala
5:131679107:C:T	missense	ENST00000510461.6:c.1271G>A	ENSP00000421985.1:p.Gly424 Glu
5:131679110:G:A	missense	ENST00000510461.6:c.1268C>T	ENSP00000421985.1:p.Ser423 Leu
5:131679112:C:T	missense	ENST00000510461.6:c.1266G>A	ENSP00000421985.1:p.Met42 2Ile
5:131679113:A:G	missense	ENST00000510461.6:c.1265T>C	ENSP00000421985.1:p.Met42 2Thr
5:131679114:T:A	missense	ENST00000510461.6:c.1264A>T	ENSP00000421985.1:p.Met42 2Leu
5:131679117:T:A	missense	ENST00000510461.6:c.1261A>T	ENSP00000421985.1:p.Met42 1Leu
5:131679117:T:C	missense	ENST00000510461.6:c.1261A>G	ENSP00000421985.1:p.Met42 1Val
5:131679119:G:T	missense	ENST00000510461.6:c.1259C>A	ENSP00000421985.1:p.Thr420 Lys
5:131679120:T:C	missense	ENST00000510461.6:c.1258A>G	ENSP00000421985.1:p.Thr420 Ala
5:131679124:C:T	stop_gained	ENST00000510461.6:c.1254G>A	ENSP00000421985.1:p.Trp418 Ter
5:131679126:A:G	missense	ENST00000510461.6:c.1252T>C	ENSP00000421985.1:p.Trp418 Arg
5:131679129:C:G	missense	ENST00000510461.6:c.1249G>C	ENSP00000421985.1:p.Val417 Leu
5:131679129:C:T	missense	ENST00000510461.6:c.1249G>A	ENSP00000421985.1:p.Val417 Ile
5:131679131:G:T	missense	ENST00000510461.6:c.1247C>A	ENSP00000421985.1:p.Pro416 His
5:131679132:G:A	missense	ENST00000510461.6:c.1246C>T	ENSP00000421985.1:p.Pro416 Ser
5:131679132:G:T	missense	ENST00000510461.6:c.1246C>A	ENSP00000421985.1:p.Pro416 Thr

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5:131679133:T:G	missense	ENST00000510461.6:c.1245A>C	ENSP00000421985.1:p.Glu415 Asp
5:131679135:C:T	missense	ENST00000510461.6:c.1243G>A	ENSP00000421985.1:p.Glu415 Lys
5:131679138:C:A	stop_gain ed	ENST00000510461.6:c.1240G>T	ENSP00000421985.1:p.Gly414 Ter
5:131679138:C:T	missense	ENST00000510461.6:c.1240G>A	ENSP00000421985.1:p.Gly414 Arg
5:131679143:C:T	missense	ENST00000510461.6:c.1235G>A	ENSP00000421985.1:p.Arg412 Gln
5:131679144:G:A	stop_gain ed	ENST00000510461.6:c.1234C>T	ENSP00000421985.1:p.Arg412 Ter
5:131679147:G:C	missense	ENST00000510461.6:c.1231C>G	ENSP00000421985.1:p.Pro411 Ala
5:131679147:G:T	missense	ENST00000510461.6:c.1231C>A	ENSP00000421985.1:p.Pro411 Thr
5:131679149:A:G	missense	ENST00000510461.6:c.1229T>C	ENSP00000421985.1:p.Met41 OThr
5:131679150:T:A	missense	ENST00000510461.6:c.1228A>T	ENSP00000421985.1:p.Met41 OLeu
5:131679152:G:A	missense	ENST00000510461.6:c.1226C>T	ENSP00000421985.1:p.Thr409 Met
5:131679152:G:T	missense	ENST00000510461.6:c.1226C>A	ENSP00000421985.1:p.Thr409 Lys
5:131679153:T:C	missense	ENST00000510461.6:c.1225A>G	ENSP00000421985.1:p.Thr409 Ala
5:131679154:G:T	stop_gain ed	ENST00000510461.6:c.1224C>A	ENSP00000421985.1:p.Tyr408 Ter
5:131679156:A:G	missense	ENST00000510461.6:c.1222T>C	ENSP00000421985.1:p.Tyr408 His
5:131679161:T:G	missense	ENST00000510461.6:c.1217A>C	ENSP00000421985.1:p.Asn406 Thr
5:131679164:C:A	missense	ENST00000510461.6:c.1214G>T	ENSP00000421985.1:p.Cys405 Phe

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5:131679164:C:G	missense	ENST00000510461.6:c.1214G>C	ENSP00000421985.1:p.Cys405 Ser
5:131679164:C:T	missense	ENST00000510461.6:c.1214G>A	ENSP00000421985.1:p.Cys405 Tyr
5:131679165:A:G	missense	ENST00000510461.6:c.1213T>C	ENSP00000421985.1:p.Cys405 Arg
5:131679168:T:C	missense	ENST00000510461.6:c.1210A>G	ENSP00000421985.1:p.Ile404 Val
5:131679170:G:A	missense	ENST00000510461.6:c.1208C>T	ENSP00000421985.1:p.Thr403 Ile
5:131679170:G:T	missense	ENST00000510461.6:c.1208C>A	ENSP00000421985.1:p.Thr403 Lys
5:131679171:T:A	missense	ENST00000510461.6:c.1207A>T	ENSP00000421985.1:p.Thr403 Ser
5:131679171:T:C	missense	ENST00000510461.6:c.1207A>G	ENSP00000421985.1:p.Thr403 Ala
5:131679173:G:C	missense	ENST00000510461.6:c.1205C>G	ENSP00000421985.1:p.Thr402 Arg
5:131679173:G:T	missense	ENST00000510461.6:c.1205C>A	ENSP00000421985.1:p.Thr402 Lys
5:131679173:GTT C:G	splice_acc eptor	ENST00000510461.6:c.1203- 1_1204del	NA
5:131679175:T:G	missense	ENST00000510461.6:c.1203A>C	ENSP00000421985.1:p.Arg401 Ser
5:131679176:C:T	splice_acc eptor	ENST00000510461.6:c.1203- 1G>A	NA
5:131679177:T:A	splice_acc eptor	ENST00000510461.6:c.1203- 2A>T	NA
5:131698916:C:T	splice_do nor	ENST00000510461.6:c.1202+1G >A	NA
5:131698919:G:C	missense	ENST00000510461.6:c.1200C>G	ENSP00000421985.1:p.Phe40 0Leu
5:131698921:A:G	missense	ENST00000510461.6:c.1198T>C	ENSP00000421985.1:p.Phe40 0Leu

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5:131698930:G:C	missense	ENST00000510461.6:c.1189C>G	ENSP00000421985.1:p.Leu397 Val
5:131698932:G:A	missense	ENST00000510461.6:c.1187C>T	ENSP00000421985.1:p.Ala396 Val
5:131698932:G:C	missense	ENST00000510461.6:c.1187C>G	ENSP00000421985.1:p.Ala396 Gly
5:131698932:G:T	missense	ENST00000510461.6:c.1187C>A	ENSP00000421985.1:p.Ala396 Asp
5:131698933:C:A	missense	ENST00000510461.6:c.1186G>T	ENSP00000421985.1:p.Ala396 Ser
5:131698936:C:A	missense	ENST00000510461.6:c.1183G>T	ENSP00000421985.1:p.Asp395 Tyr
5:131698936:C:T	missense	ENST00000510461.6:c.1183G>A	ENSP00000421985.1:p.Asp395 Asn
5:131698942:T:C	missense	ENST00000510461.6:c.1177A>G	ENSP00000421985.1:p.Ile393 Val
5:131698944:C:A	missense	ENST00000510461.6:c.1175G>T	ENSP00000421985.1:p.Arg392 Leu
5:131698944:C:G	missense	ENST00000510461.6:c.1175G>C	ENSP00000421985.1:p.Arg392 Pro
5:131698944:C:T	missense	ENST00000510461.6:c.1175G>A	ENSP00000421985.1:p.Arg392 Gln
5:131698945:G:A	stop_gain ed	ENST00000510461.6:c.1174C>T	ENSP00000421985.1:p.Arg392 Ter
5:131698947:T:A	missense	ENST00000510461.6:c.1172A>T	ENSP00000421985.1:p.Asn391 Ile
5:131698950:T:A	missense	ENST00000510461.6:c.1169A>T	ENSP00000421985.1:p.Tyr390 Phe
5:131698950:T:C	missense	ENST00000510461.6:c.1169A>G	ENSP00000421985.1:p.Tyr390 Cys
5:131698951:A:G	missense	ENST00000510461.6:c.1168T>C	ENSP00000421985.1:p.Tyr390 His
5:131698953:G:A	missense	ENST00000510461.6:c.1166C>T	ENSP00000421985.1:p.Ala389 Val

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5:131698959:C:G	missense	ENST00000510461.6:c.1160G>C	ENSP00000421985.1:p.Ser387 Thr
5:131698963:T:C	missense	ENST00000510461.6:c.1156A>G	ENSP00000421985.1:p.Arg386 Gly
5:131698967:A:T	missense	ENST00000510461.6:c.1152T>A	ENSP00000421985.1:p.Ser384 Arg
5:131698968:C:A	missense	ENST00000510461.6:c.1151G>T	ENSP00000421985.1:p.Ser384 Ile
5:131698968:C:G	missense	ENST00000510461.6:c.1151G>C	ENSP00000421985.1:p.Ser384 Thr
5:131698969:T:C	missense	ENST00000510461.6:c.1150A>G	ENSP00000421985.1:p.Ser384 Gly
5:131698972:C:T	missense	ENST00000510461.6:c.1147G>A	ENSP00000421985.1:p.Ala383 Thr
5:131698974:T:C	missense	ENST00000510461.6:c.1145A>G	ENSP00000421985.1:p.Asp382 Gly
5:131698978:C:G	missense	ENST00000510461.6:c.1141G>C	ENSP00000421985.1:p.Ala381 Pro
5:131698979:TG: T	frameshift	ENST00000510461.6:c.1139del	ENSP00000421985.1:p.Ser380 Ter
5:131698981:A:C	missense	ENST00000510461.6:c.1138T>G	ENSP00000421985.1:p.Ser380 Ala
5:131698981:A:G	missense	ENST00000510461.6:c.1138T>C	ENSP00000421985.1:p.Ser380 Pro
5:131698983:C:T	missense	ENST00000510461.6:c.1136G>A	ENSP00000421985.1:p.Arg379 Lys
5:131698984:T:C	missense	ENST00000510461.6:c.1135A>G	ENSP00000421985.1:p.Arg379 Gly
5:131698986:C:T	missense	ENST00000510461.6:c.1133G>A	ENSP00000421985.1:p.Arg378 Gln
5:131698987:G:A	missense	ENST00000510461.6:c.1132C>T	ENSP00000421985.1:p.Arg378 Trp
5:131698991:C:T	missense	ENST00000510461.6:c.1128G>A	ENSP00000421985.1:p.Met37 Ile

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5:131698993:T:C	missense	ENST00000510461.6:c.1126A>G	ENSP00000421985.1:p.Met37 6Val
5:131698997:C:G	missense	ENST00000510461.6:c.1122G>C	ENSP00000421985.1:p.Met37 4Ile
5:131698998:A:G	missense	ENST00000510461.6:c.1121T>C	ENSP00000421985.1:p.Met37 4Thr
5:131698999:T:C	missense	ENST00000510461.6:c.1120A>G	ENSP00000421985.1:p.Met37 4Val
5:131699001:G:A	missense	ENST00000510461.6:c.1118C>T	ENSP00000421985.1:p.Ala373 Val
5:131699001:G:T	missense	ENST00000510461.6:c.1118C>A	ENSP00000421985.1:p.Ala373 Asp
5:131704062:TA: T	splice_do nor	ENST00000510461.6:c.1116+2d el	NA
5:131704072:A:G	missense	ENST00000510461.6:c.1109T>C	ENSP00000421985.1:p.Ile370T hr
5:131704073:T:C	missense	ENST00000510461.6:c.1108A>G	ENSP00000421985.1:p.Ile370 Val
5:131704075:G:A	missense	ENST00000510461.6:c.1106C>T	ENSP00000421985.1:p.Ala369 Val
5:131704079:T:A	missense	ENST00000510461.6:c.1102A>T	ENSP00000421985.1:p.Ser368 Cys
5:131704081:T:C	missense	ENST00000510461.6:c.1100A>G	ENSP00000421985.1:p.Lys367 Arg
5:131704090:T:C	missense	ENST00000510461.6:c.1091A>G	ENSP00000421985.1:p.Asn364 Ser
5:131704094:T:C	missense	ENST00000510461.6:c.1087A>G	ENSP00000421985.1:p.Met36 3Val
5:131704096:T:A	missense	ENST00000510461.6:c.1085A>T	ENSP00000421985.1:p.His362 Leu
5:131704099:C:T	missense	ENST00000510461.6:c.1082G>A	ENSP00000421985.1:p.Ser361 Asn
5:131704108:A:T	missense	ENST00000510461.6:c.1073T>A	ENSP00000421985.1:p.Leu358 His

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5:131704109:G:C	missense	ENST00000510461.6:c.1072C>G	ENSP00000421985.1:p.Leu358 Val
5:131704111:G:A	missense	ENST00000510461.6:c.1070C>T	ENSP00000421985.1:p.Pro357 Leu
5:131704112:G:A	missense	ENST00000510461.6:c.1069C>T	ENSP00000421985.1:p.Pro357 Ser
5:131704114:A:C	missense	ENST00000510461.6:c.1067T>G	ENSP00000421985.1:p.Phe35 6Cys
5:131704120:G:G A	frameshift	ENST00000510461.6:c.1060dup	ENSP00000421985.1:p.Ser354 PhefsTer7
5:131704124:A:G	missense	ENST00000510461.6:c.1057T>C	ENSP00000421985.1:p.Phe35 3Leu
5:131704127:A:G	missense	ENST00000510461.6:c.1054T>C	ENSP00000421985.1:p.Phe35 2Leu
5:131704128:G:T	missense	ENST00000510461.6:c.1053C>A	ENSP00000421985.1:p.Phe35 1Leu
5:131704130:A:C	missense	ENST00000510461.6:c.1051T>G	ENSP00000421985.1:p.Phe35 1Val
5:131704131:T:A	missense	ENST00000510461.6:c.1050A>T	ENSP00000421985.1:p.Glu350 Asp
5:131704132:T:A	missense	ENST00000510461.6:c.1049A>T	ENSP00000421985.1:p.Glu350 Val
5:131704135:T:C	missense	ENST00000510461.6:c.1046A>G	ENSP00000421985.1:p.Asn349 Ser
5:131704137:A:C	missense	ENST00000510461.6:c.1044T>G	ENSP00000421985.1:p.Phe34 8Leu
5:131704138:A:G	missense	ENST00000510461.6:c.1043T>C	ENSP00000421985.1:p.Phe34 8Ser
5:131704138:A:T	missense	ENST00000510461.6:c.1043T>A	ENSP00000421985.1:p.Phe34 8Tyr
5:131704140:T:G	missense	ENST00000510461.6:c.1041A>C	ENSP00000421985.1:p.Lys347 Asn
5:131704141:T:G	missense	ENST00000510461.6:c.1040A>C	ENSP00000421985.1:p.Lys347 Thr

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5:131704142:T:C	missense	ENST00000510461.6:c.1039A>G	ENSP00000421985.1:p.Lys347 Glu
5:131704144:T:C	missense	ENST00000510461.6:c.1037A>G	ENSP00000421985.1:p.Asn346 Ser
5:131704147:T:C	missense	ENST00000510461.6:c.1034A>G	ENSP00000421985.1:p.Asn345 Ser
5:131704153:T:A	missense	ENST00000510461.6:c.1028A>T	ENSP00000421985.1:p.Asp343 Val
5:131704157:C:T	missense	ENST00000510461.6:c.1024G>A	ENSP00000421985.1:p.Glu342 Lys
5:131704159:T:A	missense	ENST00000510461.6:c.1022A>T	ENSP00000421985.1:p.Asp341 Val
5:131704160:CT:C	frameshift	ENST00000510461.6:c.1020del	ENSP00000421985.1:p.Asp341 MetfsTer23
5:131704162:T:C	missense	ENST00000510461.6:c.1019A>G	ENSP00000421985.1:p.Lys340 Arg
5:131704165:G:C	missense	ENST00000510461.6:c.1016C>G	ENSP00000421985.1:p.Ser339 Cys
5:131704166:A:G	missense	ENST00000510461.6:c.1015T>C	ENSP00000421985.1:p.Ser339 Pro
5:131704167:C:G	missense	ENST00000510461.6:c.1014G>C	ENSP00000421985.1:p.Leu338 Phe
5:131704171:G:A	missense	ENST00000510461.6:c.1010C>T	ENSP00000421985.1:p.Ser337 Leu
5:131704178:T:A	missense	ENST00000510461.6:c.1003A>T	ENSP00000421985.1:p.Ile335P he
5:131704178:T:C	missense	ENST00000510461.6:c.1003A>G	ENSP00000421985.1:p.Ile335 Val
5:131704181:C:A	missense	ENST00000510461.6:c.1000G>T	ENSP00000421985.1:p.Val334 Leu
5:131704186:A:G	missense	ENST00000510461.6:c.995T>C	ENSP00000421985.1:p.Ile332T hr
5:131704187:T:C	missense	ENST00000510461.6:c.994A>G	ENSP00000421985.1:p.Ile332 Val

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5:131704193:T:C	missense	ENST00000510461.6:c.988A>G	ENSP00000421985.1:p.Ile330 Val
5:131704202:T:G	missense	ENST00000510461.6:c.979A>C	ENSP00000421985.1:p.Lys327 Gln
5:131704204:C:T	missense	ENST00000510461.6:c.977G>A	ENSP00000421985.1:p.Arg326 Gln
5:131704205:G:A	missense	ENST00000510461.6:c.976C>T	ENSP00000421985.1:p.Arg326 Trp
5:131704207:A:C	missense	ENST00000510461.6:c.974T>G	ENSP00000421985.1:p.Val325 Gly
5:131704207:A:G	missense	ENST00000510461.6:c.974T>C	ENSP00000421985.1:p.Val325 Ala
5:131704208:C:T	missense	ENST00000510461.6:c.973G>A	ENSP00000421985.1:p.Val325 Met
5:131704211:T:C	missense	ENST00000510461.6:c.970A>G	ENSP00000421985.1:p.Ile324 Val
5:131704214:C:T	missense	ENST00000510461.6:c.967G>A	ENSP00000421985.1:p.Gly323 Arg
5:131704216:G:A	missense	ENST00000510461.6:c.965C>T	ENSP00000421985.1:p.Pro322 Leu
5:131704220:T:G	missense	ENST00000510461.6:c.961A>C	ENSP00000421985.1:p.Asn321 His
5:131704222:G:A	missense	ENST00000510461.6:c.959C>T	ENSP00000421985.1:p.Pro320 Leu
5:131704222:G:T	missense	ENST00000510461.6:c.959C>A	ENSP00000421985.1:p.Pro320 His
5:131704223:G:A	missense	ENST00000510461.6:c.958C>T	ENSP00000421985.1:p.Pro320 Ser
5:131704228:C:G	missense	ENST00000510461.6:c.953G>C	ENSP00000421985.1:p.Cys318 Ser
5:131704228:C:T	missense	ENST00000510461.6:c.953G>A	ENSP00000421985.1:p.Cys318 Tyr
5:131704229:A:G	missense	ENST00000510461.6:c.952T>C	ENSP00000421985.1:p.Cys318 Arg

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5:131704230:G:C	missense	ENST00000510461.6:c.951C>G	ENSP00000421985.1:p.Ser317 Arg
5:131704231:C:T	missense	ENST00000510461.6:c.950G>A	ENSP00000421985.1:p.Ser317 Asn
5:131704232:T:G	missense	ENST00000510461.6:c.949A>C	ENSP00000421985.1:p.Ser317 Arg
5:131704236:A:T	missense	ENST00000510461.6:c.945T>A	ENSP00000421985.1:p.Asp315 Glu
5:131704237:T:A	missense	ENST00000510461.6:c.944A>T	ENSP00000421985.1:p.Asp315 Val
5:131704237:T:C	missense	ENST00000510461.6:c.944A>G	ENSP00000421985.1:p.Asp315 Gly
5:131704240:G:A	missense	ENST00000510461.6:c.941C>T	ENSP00000421985.1:p.Ser314 Leu
5:131704250:A:G	missense	ENST00000510461.6:c.931T>C	ENSP00000421985.1:p.Phe311 1Leu
5:131704251:G:C	missense	ENST00000510461.6:c.930C>G	ENSP00000421985.1:p.Ser310 Arg
5:131704252:C:T	missense	ENST00000510461.6:c.929G>A	ENSP00000421985.1:p.Ser310 Asn
5:131704259:C:T	missense	ENST00000510461.6:c.922G>A	ENSP00000421985.1:p.Glu308 Lys
5:131704261:A:G	missense	ENST00000510461.6:c.920T>C	ENSP00000421985.1:p.Ile307T hr
5:131704262:T:C	missense	ENST00000510461.6:c.919A>G	ENSP00000421985.1:p.Ile307 Val
5:131706409:A:G	splice_do nor	ENST00000510461.6:c.914+2T> C	NA
5:131706412:A:G	missense	ENST00000510461.6:c.913T>C	ENSP00000421985.1:p.Trp305 Arg
5:131706414:C:T	missense	ENST00000510461.6:c.911G>A	ENSP00000421985.1:p.Arg304 Lys
5:131706418:G:A	missense	ENST00000510461.6:c.907C>T	ENSP00000421985.1:p.Pro303 Ser

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5:131706424:C:T	missense	ENST00000510461.6:c.901G>A	ENSP00000421985.1:p.Val301Ile
5:131706426:C:G	missense	ENST00000510461.6:c.899G>C	ENSP00000421985.1:p.Gly300Ala
5:131706426:C:T	missense	ENST00000510461.6:c.899G>A	ENSP00000421985.1:p.Gly300Glu
5:131706427:C:T	missense	ENST00000510461.6:c.898G>A	ENSP00000421985.1:p.Gly300Arg
5:131706432:T:C	missense	ENST00000510461.6:c.893A>G	ENSP00000421985.1:p.Glu298Gly
5:131706438:C:G	missense	ENST00000510461.6:c.887G>C	ENSP00000421985.1:p.Ser296Thr
5:131706441:G:C	missense	ENST00000510461.6:c.884C>G	ENSP00000421985.1:p.Thr295Arg
5:131706442:T:C	missense	ENST00000510461.6:c.883A>G	ENSP00000421985.1:p.Thr295Ala
5:131706445:T:C	missense	ENST00000510461.6:c.880A>G	ENSP00000421985.1:p.Thr294Ala
5:131706448:G:C	missense	ENST00000510461.6:c.877C>G	ENSP00000421985.1:p.Gln293Glu
5:131706453:C:T	missense	ENST00000510461.6:c.872G>A	ENSP00000421985.1:p.Arg291His
5:131706454:G:A	missense	ENST00000510461.6:c.871C>T	ENSP00000421985.1:p.Arg291Cys
5:131706456:C:T	missense	ENST00000510461.6:c.869G>A	ENSP00000421985.1:p.Arg290Gln
5:131706457:G:A	stop_gained	ENST00000510461.6:c.868C>T	ENSP00000421985.1:p.Arg290Ter
5:131706462:C:T	missense	ENST00000510461.6:c.863G>A	ENSP00000421985.1:p.Arg288His
5:131706463:G:A	missense	ENST00000510461.6:c.862C>T	ENSP00000421985.1:p.Arg288Cys
5:131706463:G:T	missense	ENST00000510461.6:c.862C>A	ENSP00000421985.1:p.Arg288Ser

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5:131706465:C:T	missense	ENST00000510461.6:c.860G>A	ENSP00000421985.1:p.Arg287 Gln
5:131706466:G:A	stop_gained	ENST00000510461.6:c.859C>T	ENSP00000421985.1:p.Arg287 Ter
5:131706471:T:C	missense	ENST00000510461.6:c.854A>G	ENSP00000421985.1:p.Tyr285 Cys
5:131706480:G:A	missense	ENST00000510461.6:c.845C>T	ENSP00000421985.1:p.Ala282 Val
5:131706486:C:T	missense	ENST00000510461.6:c.839G>A	ENSP00000421985.1:p.Ser280 Asn
5:131706487:T:A	missense	ENST00000510461.6:c.838A>T	ENSP00000421985.1:p.Ser280 Cys
5:131706489:C:T	missense	ENST00000510461.6:c.836G>A	ENSP00000421985.1:p.Arg279 Gln
5:131706490:G:A	stop_gained	ENST00000510461.6:c.835C>T	ENSP00000421985.1:p.Arg279 Ter
5:131706490:G:C	missense	ENST00000510461.6:c.835C>G	ENSP00000421985.1:p.Arg279 Gly
5:131706491:GGTAA:G	frameshift	ENST00000510461.6:c.830_833del	ENSP00000421985.1:p.Leu277 ProfsTer30
5:131706501:G:A	missense	ENST00000510461.6:c.824C>T	ENSP00000421985.1:p.Ser275 Phe
5:131706502:A:C	missense	ENST00000510461.6:c.823T>G	ENSP00000421985.1:p.Ser275 Ala
5:131706504:T:G	missense	ENST00000510461.6:c.821A>C	ENSP00000421985.1:p.Asn274 Thr
5:131706507:G:C	missense	ENST00000510461.6:c.818C>G	ENSP00000421985.1:p.Pro273 Arg
5:131706508:G:C	missense	ENST00000510461.6:c.817C>G	ENSP00000421985.1:p.Pro273 Ala
5:131706516:A:C	missense	ENST00000510461.6:c.809T>G	ENSP00000421985.1:p.Phe27 OCys
5:131706519:G:A	missense	ENST00000510461.6:c.806C>T	ENSP00000421985.1:p.Pro269 Leu

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5:131706519:G:C	missense	ENST00000510461.6:c.806C>G	ENSP00000421985.1:p.Pro269 Arg
5:131706520:G:C	missense	ENST00000510461.6:c.805C>G	ENSP00000421985.1:p.Pro269 Ala
5:131706523:T:A	missense	ENST00000510461.6:c.802A>T	ENSP00000421985.1:p.Thr268 Ser
5:131706523:T:C	missense	ENST00000510461.6:c.802A>G	ENSP00000421985.1:p.Thr268 Ala
5:131706524:G:C	missense	ENST00000510461.6:c.801C>G	ENSP00000421985.1:p.Ile267 Met
5:131706525:A:G	missense	ENST00000510461.6:c.800T>C	ENSP00000421985.1:p.Ile267T hr
5:131706526:T:C	missense	ENST00000510461.6:c.799A>G	ENSP00000421985.1:p.Ile267 Val
5:131706541:G:A	missense	ENST00000510461.6:c.784C>T	ENSP00000421985.1:p.Leu262 Phe
5:131706548:T:C	splice_acc eptor	ENST00000510461.6:c.779- 2A>G	NA
5:131709206:C:T	missense	ENST00000510461.6:c.773G>A	ENSP00000421985.1:p.Arg258 Gln
5:131709207:G:A	missense	ENST00000510461.6:c.772C>T	ENSP00000421985.1:p.Arg258 Trp
5:131709210:C:A	missense	ENST00000510461.6:c.769G>T	ENSP00000421985.1:p.Ala257 Ser
5:131709210:C:G	missense	ENST00000510461.6:c.769G>C	ENSP00000421985.1:p.Ala257 Pro
5:131709210:C:T	missense	ENST00000510461.6:c.769G>A	ENSP00000421985.1:p.Ala257 Thr
5:131709213:T:C	missense	ENST00000510461.6:c.766A>G	ENSP00000421985.1:p.Ile256 Val
5:131709215:C:T	missense	ENST00000510461.6:c.764G>A	ENSP00000421985.1:p.Gly255 Asp
5:131709216:C:T	missense	ENST00000510461.6:c.763G>A	ENSP00000421985.1:p.Gly255 Ser

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5:131709218:C:G	missense	ENST00000510461.6:c.761G>C	ENSP00000421985.1:p.Ser254 Thr
5:131709219:T:A	missense	ENST00000510461.6:c.760A>T	ENSP00000421985.1:p.Ser254 Cys
5:131709219:T:C	missense	ENST00000510461.6:c.760A>G	ENSP00000421985.1:p.Ser254 Gly
5:131709226:G:C	missense	ENST00000510461.6:c.753C>G	ENSP00000421985.1:p.Asp251 Glu
5:131709227:T:C	missense	ENST00000510461.6:c.752A>G	ENSP00000421985.1:p.Asp251 Gly
5:131709228:C:A	missense	ENST00000510461.6:c.751G>T	ENSP00000421985.1:p.Asp251 Tyr
5:131709233:T:C	missense	ENST00000510461.6:c.746A>G	ENSP00000421985.1:p.Asn249 Ser
5:131709234:T:C	missense	ENST00000510461.6:c.745A>G	ENSP00000421985.1:p.Asn249 Asp
5:131709234:T:G	missense	ENST00000510461.6:c.745A>C	ENSP00000421985.1:p.Asn249 His
5:131709237:G:A	missense	ENST00000510461.6:c.742C>T	ENSP00000421985.1:p.Leu248 Phe
5:131709239:T:C	missense	ENST00000510461.6:c.740A>G	ENSP00000421985.1:p.Glu247 Gly
5:131709240:C:G	missense	ENST00000510461.6:c.739G>C	ENSP00000421985.1:p.Glu247 Gln
5:131709243:T:C	missense	ENST00000510461.6:c.736A>G	ENSP00000421985.1:p.Arg246 Gly
5:131709245:C:T	missense	ENST00000510461.6:c.734G>A	ENSP00000421985.1:p.Gly245 Glu
5:131709248:G:A	missense	ENST00000510461.6:c.731C>T	ENSP00000421985.1:p.Pro244 Leu
5:131709248:G:C	missense	ENST00000510461.6:c.731C>G	ENSP00000421985.1:p.Pro244 Arg
5:131709252:T:C	missense	ENST00000510461.6:c.727A>G	ENSP00000421985.1:p.Met24 3Val

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5:131709258:T:C	missense	ENST00000510461.6:c.721A>G	ENSP00000421985.1:p.Met241Val
5:131709258:T:G	missense	ENST00000510461.6:c.721A>C	ENSP00000421985.1:p.Met241Leu
5:131709260:G:C	missense	ENST00000510461.6:c.719C>G	ENSP00000421985.1:p.Pro240Arg
5:131709269:T:C	missense	ENST00000510461.6:c.710A>G	ENSP00000421985.1:p.His237Arg
5:131709270:G:A	missense	ENST00000510461.6:c.709C>T	ENSP00000421985.1:p.His237Tyr
5:131710581:C:A	missense	ENST00000510461.6:c.703G>T	ENSP00000421985.1:p.Ala235Ser
5:131710581:C:T	missense	ENST00000510461.6:c.703G>A	ENSP00000421985.1:p.Ala235Thr
5:131710582:A:C	missense	ENST00000510461.6:c.702T>G	ENSP00000421985.1:p.Phe234Leu
5:131710584:A:C	missense	ENST00000510461.6:c.700T>G	ENSP00000421985.1:p.Phe234Val
5:131710593:C:T	missense	ENST00000510461.6:c.691G>A	ENSP00000421985.1:p.Ala231Thr
5:131710594:G:T	missense	ENST00000510461.6:c.690C>A	ENSP00000421985.1:p.Ser230Arg
5:131710595:C:T	missense	ENST00000510461.6:c.689G>A	ENSP00000421985.1:p.Ser230Asn
5:131710600:G:C	missense	ENST00000510461.6:c.684C>G	ENSP00000421985.1:p.Ile228Met
5:131710604:A:G	missense	ENST00000510461.6:c.680T>C	ENSP00000421985.1:p.Leu227Pro
5:131710605:G:C	missense	ENST00000510461.6:c.679C>G	ENSP00000421985.1:p.Leu227Val
5:131710607:C:T	missense	ENST00000510461.6:c.677G>A	ENSP00000421985.1:p.Arg226His
5:131710608:G:A	missense	ENST00000510461.6:c.676C>T	ENSP00000421985.1:p.Arg226Cys

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5:131710610:A:C	missense	ENST00000510461.6:c.674T>G	ENSP00000421985.1:p.Leu225 Arg
5:131710613:G:A	missense	ENST00000510461.6:c.671C>T	ENSP00000421985.1:p.Pro224 Leu
5:131710613:G:T	missense	ENST00000510461.6:c.671C>A	ENSP00000421985.1:p.Pro224 Gln
5:131710614:G:C	missense	ENST00000510461.6:c.670C>G	ENSP00000421985.1:p.Pro224 Ala
5:131710617:C:T	missense	ENST00000510461.6:c.667G>A	ENSP00000421985.1:p.Gly223 Ser
5:131710618:C:G	missense	ENST00000510461.6:c.666G>C	ENSP00000421985.1:p.Gln222 His
5:131710628:A:G	missense	ENST00000510461.6:c.656T>C	ENSP00000421985.1:p.Phe21 9Ser
5:131710632:C:G	missense	ENST00000510461.6:c.652G>C	ENSP00000421985.1:p.Ala218 Pro
5:131710632:C:T	missense	ENST00000510461.6:c.652G>A	ENSP00000421985.1:p.Ala218 Thr
5:131710634:C:T	missense	ENST00000510461.6:c.650G>A	ENSP00000421985.1:p.Arg217 Gln
5:131710635:G:A	missense	ENST00000510461.6:c.649C>T	ENSP00000421985.1:p.Arg217 Trp
5:131710637:C:A	missense	ENST00000510461.6:c.647G>T	ENSP00000421985.1:p.Arg216 Met
5:131710637:C:G	missense	ENST00000510461.6:c.647G>C	ENSP00000421985.1:p.Arg216 Thr
5:131710638:T:C	missense	ENST00000510461.6:c.646A>G	ENSP00000421985.1:p.Arg216 Gly
5:131710640:G:A	missense	ENST00000510461.6:c.644C>T	ENSP00000421985.1:p.Pro215 Leu
5:131710640:G:C	missense	ENST00000510461.6:c.644C>G	ENSP00000421985.1:p.Pro215 Arg
5:131710643:C:T	missense	ENST00000510461.6:c.641G>A	ENSP00000421985.1:p.Ser214 Asn

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5:131710644:T:C	missense	ENST00000510461.6:c.640A>G	ENSP00000421985.1:p.Ser214 Gly
5:131710647:A:C	missense	ENST00000510461.6:c.637T>G	ENSP00000421985.1:p.Cys213 Gly
5:131710649:A:T	missense	ENST00000510461.6:c.635T>A	ENSP00000421985.1:p.Phe21 2Tyr
5:131710653:G:A	stop_gain ed	ENST00000510461.6:c.631C>T	ENSP00000421985.1:p.Gln211 Ter
5:131710655:G:A	missense	ENST00000510461.6:c.629C>T	ENSP00000421985.1:p.Ser210 Leu
5:131710656:A:G	missense	ENST00000510461.6:c.628T>C	ENSP00000421985.1:p.Ser210 Pro
5:131716564:C:G	splice_do nor	ENST00000510461.6:c.622+1G> C	NA
5:131716566:T:C	missense	ENST00000510461.6:c.621A>G	ENSP00000421985.1:p.Ile207 Met
5:131716567:A:G	missense	ENST00000510461.6:c.620T>C	ENSP00000421985.1:p.Ile207T hr
5:131716570:T:C	missense	ENST00000510461.6:c.617A>G	ENSP00000421985.1:p.Asn206 Ser
5:131716573:C:A	missense	ENST00000510461.6:c.614G>T	ENSP00000421985.1:p.Gly205 Val
5:131716582:C:A	missense	ENST00000510461.6:c.605G>T	ENSP00000421985.1:p.Gly202 Val
5:131716582:C:T	missense	ENST00000510461.6:c.605G>A	ENSP00000421985.1:p.Gly202 Glu
5:131716589:T:C	missense	ENST00000510461.6:c.598A>G	ENSP00000421985.1:p.Ile200 Val
5:131716592:C:A	missense	ENST00000510461.6:c.595G>T	ENSP00000421985.1:p.Val199 Phe
5:131716592:C:T	missense	ENST00000510461.6:c.595G>A	ENSP00000421985.1:p.Val199I le
5:131716592:CTG :C	frameshif t	ENST00000510461.6:c.593_594 del	ENSP00000421985.1:p.Thr198 SerfsTer3

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5:131716600:T:A	missense	ENST00000510461.6:c.587A>T	ENSP00000421985.1:p.Asn196 Ile
5:131716600:T:C	missense	ENST00000510461.6:c.587A>G	ENSP00000421985.1:p.Asn196 Ser
5:131716601:T:C	missense	ENST00000510461.6:c.586A>G	ENSP00000421985.1:p.Asn196 Asp
5:131716606:G:C	missense	ENST00000510461.6:c.581C>G	ENSP00000421985.1:p.Ala194 Gly
5:131716607:C:A	missense	ENST00000510461.6:c.580G>T	ENSP00000421985.1:p.Ala194 Ser
5:131716607:C:T	missense	ENST00000510461.6:c.580G>A	ENSP00000421985.1:p.Ala194 Thr
5:131716613:A:C	missense	ENST00000510461.6:c.574T>G	ENSP00000421985.1:p.Leu192 Val
5:131716615:G:T	missense	ENST00000510461.6:c.572C>A	ENSP00000421985.1:p.Thr191 Lys
5:131716615:GT:G	frameshift	ENST00000510461.6:c.571del	ENSP00000421985.1:p.Thr191 HisfsTer2
5:131716616:T:C	missense	ENST00000510461.6:c.571A>G	ENSP00000421985.1:p.Thr191 Ala
5:131716617:A:C	missense	ENST00000510461.6:c.570T>G	ENSP00000421985.1:p.Asn190 Lys
5:131716618:T:C	missense	ENST00000510461.6:c.569A>G	ENSP00000421985.1:p.Asn190 Ser
5:131716621:T:C	missense	ENST00000510461.6:c.566A>G	ENSP00000421985.1:p.Asn189 Ser
5:131716622:T:A	missense	ENST00000510461.6:c.565A>T	ENSP00000421985.1:p.Asn189 Tyr
5:131716627:T:C	missense	ENST00000510461.6:c.560A>G	ENSP00000421985.1:p.Gln187 Arg
5:131716630:T:A	missense	ENST00000510461.6:c.557A>T	ENSP00000421985.1:p.Asn186 Ile
5:131716630:T:C	missense	ENST00000510461.6:c.557A>G	ENSP00000421985.1:p.Asn186 Ser

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5:131716634:T:C	missense	ENST00000510461.6:c.553A>G	ENSP00000421985.1:p.Ile185 Val
5:131716634:T:G	missense	ENST00000510461.6:c.553A>C	ENSP00000421985.1:p.Ile185L eu
5:131716638:T:A	missense	ENST00000510461.6:c.549A>T	ENSP00000421985.1:p.Glu183 Asp
5:131716648:T:C	missense	ENST00000510461.6:c.539A>G	ENSP00000421985.1:p.Asp180 Gly
5:131716651:T:G	missense	ENST00000510461.6:c.536A>C	ENSP00000421985.1:p.Gln179 Pro
5:131716652:G:A	stop_gain ed	ENST00000510461.6:c.535C>T	ENSP00000421985.1:p.Gln179 Ter
5:131716655:G:T	missense	ENST00000510461.6:c.532C>A	ENSP00000421985.1:p.Leu178 Ile
5:131718984:A:T	splice_do nor	ENST00000510461.6:c.530+2T> A	NA
5:131718985:C:T	splice_do nor	ENST00000510461.6:c.530+1G> A	NA
5:131718986:G:A	missense	ENST00000510461.6:c.530C>T	ENSP00000421985.1:p.Thr177 Met
5:131718986:G:C	missense	ENST00000510461.6:c.530C>G	ENSP00000421985.1:p.Thr177 Arg
5:131718986:G:T	missense	ENST00000510461.6:c.530C>A	ENSP00000421985.1:p.Thr177 Lys
5:131718989:T:A	missense	ENST00000510461.6:c.527A>T	ENSP00000421985.1:p.Asn176 Ile
5:131718989:T:C	missense	ENST00000510461.6:c.527A>G	ENSP00000421985.1:p.Asn176 Ser
5:131718989:T:G	missense	ENST00000510461.6:c.527A>C	ENSP00000421985.1:p.Asn176 Thr
5:131718993:G:A	missense	ENST00000510461.6:c.523C>T	ENSP00000421985.1:p.Leu175 Phe
5:131718995:C:T	missense	ENST00000510461.6:c.521G>A	ENSP00000421985.1:p.Ser174 Asn

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5:131718998:C:T	missense	ENST00000510461.6:c.518G>A	ENSP00000421985.1:p.Gly173 Glu
5:131719001:C:A	missense	ENST00000510461.6:c.515G>T	ENSP00000421985.1:p.Cys172 Phe
5:131719013:C:T	missense	ENST00000510461.6:c.503G>A	ENSP00000421985.1:p.Gly168 Asp
5:131719014:C:T	missense	ENST00000510461.6:c.502G>A	ENSP00000421985.1:p.Gly168 Ser
5:131719016:G:A	missense	ENST00000510461.6:c.500C>T	ENSP00000421985.1:p.Thr167 Ile
5:131719016:G:C	missense	ENST00000510461.6:c.500C>G	ENSP00000421985.1:p.Thr167 Ser
5:131719019:C:T	missense	ENST00000510461.6:c.497G>A	ENSP00000421985.1:p.Arg166 Gln
5:131719020:G:A	missense	ENST00000510461.6:c.496C>T	ENSP00000421985.1:p.Arg166 Trp
5:131719020:G:C	missense	ENST00000510461.6:c.496C>G	ENSP00000421985.1:p.Arg166 Gly
5:131719025:G:T	missense	ENST00000510461.6:c.491C>A	ENSP00000421985.1:p.Thr164 Asn
5:131719026:T:C	missense	ENST00000510461.6:c.490A>G	ENSP00000421985.1:p.Thr164 Ala
5:131719027:A:A AACACTTTGC	frameshift	ENST00000510461.6:c.479_488 dup	ENSP00000421985.1:p.Phe16 3LeufsTer22
5:131719027:A:C	missense	ENST00000510461.6:c.489T>G	ENSP00000421985.1:p.Phe16 3Leu
5:131719031:A:G	missense	ENST00000510461.6:c.485T>C	ENSP00000421985.1:p.Val162 Ala
5:131719032:C:T	missense	ENST00000510461.6:c.484G>A	ENSP00000421985.1:p.Val162 Met
5:131719035:T:G	missense	ENST00000510461.6:c.481A>C	ENSP00000421985.1:p.Lys161 Gln
5:131719041:G:A	missense	ENST00000510461.6:c.475C>T	ENSP00000421985.1:p.Leu159 Phe

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5:131719042:C:T	missense	ENST00000510461.6:c.474G>A	ENSP00000421985.1:p.Met158Ile
5:131719043:A:C	missense	ENST00000510461.6:c.473T>G	ENSP00000421985.1:p.Met158Arg
5:131719044:T:G	missense	ENST00000510461.6:c.472A>C	ENSP00000421985.1:p.Met158Leu
5:131719046:A:G	missense	ENST00000510461.6:c.470T>C	ENSP00000421985.1:p.Leu157Pro
5:131719047:G:C	missense	ENST00000510461.6:c.469C>G	ENSP00000421985.1:p.Leu157Val
5:131719048:C:G	missense	ENST00000510461.6:c.468G>C	ENSP00000421985.1:p.Gln156His
5:131719049:T:C	missense	ENST00000510461.6:c.467A>G	ENSP00000421985.1:p.Gln156Arg
5:131719050:G:A	stop_gained	ENST00000510461.6:c.466C>T	ENSP00000421985.1:p.Gln156Ter
5:131719052:G:A	missense	ENST00000510461.6:c.464C>T	ENSP00000421985.1:p.Pro155Leu
5:131719056:G:A	missense	ENST00000510461.6:c.460C>T	ENSP00000421985.1:p.Pro154Ser
5:131719058:G:A	missense	ENST00000510461.6:c.458C>T	ENSP00000421985.1:p.Ser153Phe
5:131719058:G:T	missense	ENST00000510461.6:c.458C>A	ENSP00000421985.1:p.Ser153Tyr
5:131719317:C:T	missense	ENST00000510461.6:c.455G>A	ENSP00000421985.1:p.Arg152His
5:131719318:G:A	missense	ENST00000510461.6:c.454C>T	ENSP00000421985.1:p.Arg152Cys
5:131719318:G:C	missense	ENST00000510461.6:c.454C>G	ENSP00000421985.1:p.Arg152Gly
5:131719320:A:C	missense	ENST00000510461.6:c.452T>G	ENSP00000421985.1:p.Ile151Ser
5:131719332:T:C	missense	ENST00000510461.6:c.440A>G	ENSP00000421985.1:p.Lys147Arg

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5:131719339:T:A	missense	ENST00000510461.6:c.433A>T	ENSP00000421985.1:p.Thr145 Ser
5:131719339:T:C	missense	ENST00000510461.6:c.433A>G	ENSP00000421985.1:p.Thr145 Ala
5:131719342:A:G	missense	ENST00000510461.6:c.430T>C	ENSP00000421985.1:p.Ser144 Pro
5:131719348:T:C	missense	ENST00000510461.6:c.424A>G	ENSP00000421985.1:p.Lys142 Glu
5:131719350:T:G	missense	ENST00000510461.6:c.422A>C	ENSP00000421985.1:p.Tyr141 Ser
5:131719353:C:A	missense	ENST00000510461.6:c.419G>T	ENSP00000421985.1:p.Ser140 Ile
5:131719356:A:C	missense	ENST00000510461.6:c.416T>G	ENSP00000421985.1:p.Met13 9Arg
5:131719357:T:C	missense	ENST00000510461.6:c.415A>G	ENSP00000421985.1:p.Met13 9Val
5:131719359:G:A	missense	ENST00000510461.6:c.413C>T	ENSP00000421985.1:p.Ala138 Val
5:131719363:C:T	missense	ENST00000510461.6:c.409G>A	ENSP00000421985.1:p.Val137I le
5:131719366:A:G	missense	ENST00000510461.6:c.406T>C	ENSP00000421985.1:p.Ser136 Pro
5:131719368:C:A	missense	ENST00000510461.6:c.404G>T	ENSP00000421985.1:p.Gly135 Val
5:131719368:C:G	missense	ENST00000510461.6:c.404G>C	ENSP00000421985.1:p.Gly135 Ala
5:131719374:A:G	missense	ENST00000510461.6:c.398T>C	ENSP00000421985.1:p.Met13 3Thr
5:131719375:T:C	missense	ENST00000510461.6:c.397A>G	ENSP00000421985.1:p.Met13 3Val
5:131719388:C:T	missense	ENST00000510461.6:c.384G>A	ENSP00000421985.1:p.Met12 8Ile
5:131719390:T:C	missense	ENST00000510461.6:c.382A>G	ENSP00000421985.1:p.Met12 8Val

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5:131719392:T:C	missense	ENST00000510461.6:c.380A>G	ENSP00000421985.1:p.Asn127 Ser
5:131719393:T:C	missense	ENST00000510461.6:c.379A>G	ENSP00000421985.1:p.Asn127 Asp
5:131719396:C:T	missense	ENST00000510461.6:c.376G>A	ENSP00000421985.1:p.Ala126 Thr
5:131719402:A:G	missense	ENST00000510461.6:c.370T>C	ENSP00000421985.1:p.Ser124 Pro
5:131719404:G:A	missense	ENST00000510461.6:c.368C>T	ENSP00000421985.1:p.Ser123 Phe
5:131719405:A:G	missense	ENST00000510461.6:c.367T>C	ENSP00000421985.1:p.Ser123 Pro
5:131719407:C:A	missense	ENST00000510461.6:c.365G>T	ENSP00000421985.1:p.Cys122 Phe
5:131719410:C:T	missense	ENST00000510461.6:c.362G>A	ENSP00000421985.1:p.Arg121 Gln
5:131719411:G:A	missense	ENST00000510461.6:c.361C>T	ENSP00000421985.1:p.Arg121 Trp
5:131719415:AC: A	frameshift	ENST00000510461.6:c.356del	ENSP00000421985.1:p.Gly119 ValfsTer14
5:131719416:C:T	missense	ENST00000510461.6:c.356G>A	ENSP00000421985.1:p.Gly119 Asp
5:131719417:C:G	missense	ENST00000510461.6:c.355G>C	ENSP00000421985.1:p.Gly119 Arg
5:131730903:C:G	splice_donor	ENST00000510461.6:c.354+1G> C	NA
5:131730906:G:T	missense	ENST00000510461.6:c.352C>A	ENSP00000421985.1:p.Gln118 Lys
5:131730908:T:C	missense	ENST00000510461.6:c.350A>G	ENSP00000421985.1:p.Tyr117 Cys
5:131730909:A:G	missense	ENST00000510461.6:c.349T>C	ENSP00000421985.1:p.Tyr117 His
5:131730915:G:C	missense	ENST00000510461.6:c.343C>G	ENSP00000421985.1:p.Leu115 Val

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5:131730917:C:T	missense	ENST00000510461.6:c.341G>A	ENSP00000421985.1:p.Cys114 Tyr
5:131730921:G:C	missense	ENST00000510461.6:c.337C>G	ENSP00000421985.1:p.Gln113 Glu
5:131730921:G:T	missense	ENST00000510461.6:c.337C>A	ENSP00000421985.1:p.Gln113 Lys
5:131730922:G:C	missense	ENST00000510461.6:c.336C>G	ENSP00000421985.1:p.Asp112 Glu
5:131730922:G:T	missense	ENST00000510461.6:c.336C>A	ENSP00000421985.1:p.Asp112 Glu
5:131730924:C:G	missense	ENST00000510461.6:c.334G>C	ENSP00000421985.1:p.Asp112 His
5:131730926:T:A	missense	ENST00000510461.6:c.332A>T	ENSP00000421985.1:p.Lys111 Ile
5:131730927:T:C	missense	ENST00000510461.6:c.331A>G	ENSP00000421985.1:p.Lys111 Glu
5:131730929:A:G	missense	ENST00000510461.6:c.329T>C	ENSP00000421985.1:p.Ile110T Thr
5:131730932:T:C	missense	ENST00000510461.6:c.326A>G	ENSP00000421985.1:p.Asp109 Gly
5:131730933:C:A	missense	ENST00000510461.6:c.325G>T	ENSP00000421985.1:p.Asp109 Tyr
5:131730933:C:G	missense	ENST00000510461.6:c.325G>C	ENSP00000421985.1:p.Asp109 His
5:131730935:G:C	missense	ENST00000510461.6:c.323C>G	ENSP00000421985.1:p.Ser108 Cys
5:131730936:A:C	missense	ENST00000510461.6:c.322T>G	ENSP00000421985.1:p.Ser108 Ala
5:131730938:G:T	missense	ENST00000510461.6:c.320C>A	ENSP00000421985.1:p.Ser107 Tyr
5:131730939:A:G	missense	ENST00000510461.6:c.319T>C	ENSP00000421985.1:p.Ser107 Pro
5:131730945:T:C	missense	ENST00000510461.6:c.313A>G	ENSP00000421985.1:p.Thr105 Ala

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5:131730948:C:A	missense	ENST00000510461.6:c.310G>T	ENSP00000421985.1:p.Val104 Leu
5:131730948:C:G	missense	ENST00000510461.6:c.310G>C	ENSP00000421985.1:p.Val104 Leu
5:131730948:C:T	missense	ENST00000510461.6:c.310G>A	ENSP00000421985.1:p.Val104 Met
5:131730950:G:C	missense	ENST00000510461.6:c.308C>G	ENSP00000421985.1:p.Ser103 Cys
5:131730950:G:T	missense	ENST00000510461.6:c.308C>A	ENSP00000421985.1:p.Ser103 Tyr
5:131730950:GA ACT:G	frameshift	ENST00000510461.6:c.304_307 del	ENSP00000421985.1:p.Ser102 LeufsTer2
5:131730952:A:C	missense	ENST00000510461.6:c.306T>G	ENSP00000421985.1:p.Ser102 Arg
5:131730952:A:T	missense	ENST00000510461.6:c.306T>A	ENSP00000421985.1:p.Ser102 Arg
5:131730953:C:A	missense	ENST00000510461.6:c.305G>T	ENSP00000421985.1:p.Ser102 Ile
5:131730956:T:C	missense	ENST00000510461.6:c.302A>G	ENSP00000421985.1:p.Asp101 Gly
5:131730957:C:A	missense	ENST00000510461.6:c.301G>T	ENSP00000421985.1:p.Asp101 Tyr
5:131730959:A:G	missense	ENST00000510461.6:c.299T>C	ENSP00000421985.1:p.Leu100 Ser
5:131730960:A:C	missense	ENST00000510461.6:c.298T>G	ENSP00000421985.1:p.Leu100 Val
5:131730965:G:C	missense	ENST00000510461.6:c.293C>G	ENSP00000421985.1:p.Ser98C ys
5:131730968:G:T	missense	ENST00000510461.6:c.290C>A	ENSP00000421985.1:p.Ser97T yr
5:131730969:A:T	missense	ENST00000510461.6:c.289T>A	ENSP00000421985.1:p.Ser97T hr
5:131730971:C:G	missense	ENST00000510461.6:c.287G>C	ENSP00000421985.1:p.Ser96T hr

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5:131730971:C:T	missense	ENST00000510461.6:c.287G>A	ENSP00000421985.1:p.Ser96A sn
5:131730972:T:C	missense	ENST00000510461.6:c.286A>G	ENSP00000421985.1:p.Ser96G ly
5:131730972:T:G	missense	ENST00000510461.6:c.286A>C	ENSP00000421985.1:p.Ser96A rg
5:131730974:T:C	missense	ENST00000510461.6:c.284A>G	ENSP00000421985.1:p.Asp95 Gly
5:131730975:C:T	missense	ENST00000510461.6:c.283G>A	ENSP00000421985.1:p.Asp95 Asn
5:131730978:C:A	stop_gain ed	ENST00000510461.6:c.280G>T	ENSP00000421985.1:p.Gly94T er
5:131730978:C:T	missense	ENST00000510461.6:c.280G>A	ENSP00000421985.1:p.Gly94A rg
5:131730980:C:T	missense	ENST00000510461.6:c.278G>A	ENSP00000421985.1:p.Gly93G lu
5:131730981:C:T	missense	ENST00000510461.6:c.277G>A	ENSP00000421985.1:p.Gly93A rg
5:131730983:G:A	missense	ENST00000510461.6:c.275C>T	ENSP00000421985.1:p.Pro92L eu
5:131730984:G:C	missense	ENST00000510461.6:c.274C>G	ENSP00000421985.1:p.Pro92A la
5:131730986:T:G	missense	ENST00000510461.6:c.272A>C	ENSP00000421985.1:p.Lys91T hr
5:131730987:T:G	missense	ENST00000510461.6:c.271A>C	ENSP00000421985.1:p.Lys91G ln
5:131730989:A:G	missense	ENST00000510461.6:c.269T>C	ENSP00000421985.1:p.Leu90P ro
5:131730991:T:G	missense	ENST00000510461.6:c.267A>C	ENSP00000421985.1:p.Gln89H is
5:131730992:T:C	missense	ENST00000510461.6:c.266A>G	ENSP00000421985.1:p.Gln89A rg
5:131730993:G:A	stop_gain ed	ENST00000510461.6:c.265C>T	ENSP00000421985.1:p.Gln89T er

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5:131730995:C:T	missense	ENST00000510461.6:c.263G>A	ENSP00000421985.1:p.Cys88T yr
5:131730999:A:G	missense	ENST00000510461.6:c.259T>C	ENSP00000421985.1:p.Cys87A rg
5:131731001:T:C	missense	ENST00000510461.6:c.257A>G	ENSP00000421985.1:p.Lys86A rg
5:131731004:C:A	missense	ENST00000510461.6:c.254G>T	ENSP00000421985.1:p.Gly85V al
5:131731004:C:G	missense	ENST00000510461.6:c.254G>C	ENSP00000421985.1:p.Gly85A la
5:131731007:A:C	missense	ENST00000510461.6:c.251T>G	ENSP00000421985.1:p.Phe84 Cys
5:131731010:A:C	missense	ENST00000510461.6:c.248T>G	ENSP00000421985.1:p.Val83G ly
5:131731011:C:A	missense	ENST00000510461.6:c.247G>T	ENSP00000421985.1:p.Val83P he
5:131731011:C:T	missense	ENST00000510461.6:c.247G>A	ENSP00000421985.1:p.Val83I e
5:131731014:T:C	missense	ENST00000510461.6:c.244A>G	ENSP00000421985.1:p.Lys82G lu
5:131731016:A:T	missense	ENST00000510461.6:c.242T>A	ENSP00000421985.1:p.Val81A sp
5:131731019:T:G	missense	ENST00000510461.6:c.239A>C	ENSP00000421985.1:p.Gln80P ro
5:131731020:G:A	stop_gain ed	ENST00000510461.6:c.238C>T	ENSP00000421985.1:p.Gln80T er
5:131731022:G:C	missense	ENST00000510461.6:c.236C>G	ENSP00000421985.1:p.Ala79G ly
5:131731023:C:T	missense	ENST00000510461.6:c.235G>A	ENSP00000421985.1:p.Ala79T hr
5:131731026:C:T	missense	ENST00000510461.6:c.232G>A	ENSP00000421985.1:p.Asp78 Asn
5:131731028:C:T	missense	ENST00000510461.6:c.230G>A	ENSP00000421985.1:p.Ser77A sn

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5:131731029:T:C	missense	ENST00000510461.6:c.229A>G	ENSP00000421985.1:p.Ser77Gly
5:131731031:C:A	missense	ENST00000510461.6:c.227G>T	ENSP00000421985.1:p.Gly76Val
5:131731035:G:C	missense	ENST00000510461.6:c.223C>G	ENSP00000421985.1:p.Leu75Val
5:131731039:C:G	splice_acceptor	ENST00000510461.6:c.220-1G>C	NA
5:131731040:T:C	splice_acceptor	ENST00000510461.6:c.220-2A>G	NA
5:131744563:C:A	splice_donor	ENST00000510461.6:c.219+1G>T	NA
5:131744565:G:A	missense	ENST00000510461.6:c.218C>T	ENSP00000421985.1:p.Ser73Leu
5:131744565:G:T	stop_gained	ENST00000510461.6:c.218C>A	ENSP00000421985.1:p.Ser73Ter
5:131744568:A:T	missense	ENST00000510461.6:c.215T>A	ENSP00000421985.1:p.Val72Glu
5:131744569:C:T	missense	ENST00000510461.6:c.214G>A	ENSP00000421985.1:p.Val72Ile
5:131744571:G:A	missense	ENST00000510461.6:c.212C>T	ENSP00000421985.1:p.Ser71Leu
5:131744572:A:A T	frameshift	ENST00000510461.6:c.210dup	ENSP00000421985.1:p.Ser71IlefsTer8
5:131744572:A:G	missense	ENST00000510461.6:c.211T>C	ENSP00000421985.1:p.Ser71Pro
5:131744577:T:A	missense	ENST00000510461.6:c.206A>T	ENSP00000421985.1:p.Asp69Val
5:131744577:T:C	missense	ENST00000510461.6:c.206A>G	ENSP00000421985.1:p.Asp69Gly
5:131744578:C:A	missense	ENST00000510461.6:c.205G>T	ENSP00000421985.1:p.Asp69Tyr
5:131744578:C:T	missense	ENST00000510461.6:c.205G>A	ENSP00000421985.1:p.Asp69Asn

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5:131744590:T:C	missense	ENST00000510461.6:c.193A>G	ENSP00000421985.1:p.Arg65Gly
5:131744596:C:T	missense	ENST00000510461.6:c.187G>A	ENSP00000421985.1:p.Val63Ile
5:131744598:C:A	missense	ENST00000510461.6:c.185G>T	ENSP00000421985.1:p.Ser62Ile
5:131744599:T:C	missense	ENST00000510461.6:c.184A>G	ENSP00000421985.1:p.Ser62Gly
5:131744601:G:C	missense	ENST00000510461.6:c.182C>G	ENSP00000421985.1:p.Ser61Cys
5:131744605:C:G	missense	ENST00000510461.6:c.178G>C	ENSP00000421985.1:p.Asp60His
5:131744613:A:G	missense	ENST00000510461.6:c.170T>C	ENSP00000421985.1:p.Val57Ala
5:131744616:T:C	missense	ENST00000510461.6:c.167A>G	ENSP00000421985.1:p.Asn56Ser
5:131744617:T:G	missense	ENST00000510461.6:c.166A>C	ENSP00000421985.1:p.Asn56His
5:131744623:C:A	missense	ENST00000510461.6:c.160G>T	ENSP00000421985.1:p.Gly54Trp
5:131744623:C:G	missense	ENST00000510461.6:c.160G>C	ENSP00000421985.1:p.Gly54Arg
5:131744623:C:T	missense	ENST00000510461.6:c.160G>A	ENSP00000421985.1:p.Gly54Arg
5:131744623:CT:C	frameshift	ENST00000510461.6:c.159del	ENSP00000421985.1:p.Arg55GlufsTer36
5:131744625:C:T	missense	ENST00000510461.6:c.158G>A	ENSP00000421985.1:p.Arg53Gln
5:131744626:G:A	stop_gained	ENST00000510461.6:c.157C>T	ENSP00000421985.1:p.Arg53Ter
5:131744626:G:C	missense	ENST00000510461.6:c.157C>G	ENSP00000421985.1:p.Arg53Gly
5:131744629:T:C	missense	ENST00000510461.6:c.154A>G	ENSP00000421985.1:p.Arg52Gly

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5:131744632:C:T	missense	ENST00000510461.6:c.151G>A	ENSP00000421985.1:p.Glu51Lys
5:131744634:C:G	missense	ENST00000510461.6:c.149G>C	ENSP00000421985.1:p.Cys50Ser
5:131744634:C:T	missense	ENST00000510461.6:c.149G>A	ENSP00000421985.1:p.Cys50Tyr
5:131744635:A:G	missense	ENST00000510461.6:c.148T>C	ENSP00000421985.1:p.Cys50Arg
5:131744642:A:C	stop_gain ed	ENST00000510461.6:c.141T>G	ENSP00000421985.1:p.Tyr47Ter
5:131744644:A:A T	frameshif t	ENST00000510461.6:c.138dup	ENSP00000421985.1:p.Tyr47IlefsTer5
5:131744646:A:G	missense	ENST00000510461.6:c.137T>C	ENSP00000421985.1:p.Val46Ala
5:131744647:C:T	missense	ENST00000510461.6:c.136G>A	ENSP00000421985.1:p.Val46Ile
5:131744648:A:C	missense	ENST00000510461.6:c.135T>G	ENSP00000421985.1:p.Ile45Met
5:131744650:T:C	missense	ENST00000510461.6:c.133A>G	ENSP00000421985.1:p.Ile45Val
5:131744655:C:T	missense	ENST00000510461.6:c.128G>A	ENSP00000421985.1:p.Arg43Gln
5:131744656:G:A	stop_gain ed	ENST00000510461.6:c.127C>T	ENSP00000421985.1:p.Arg43Ter
5:131744658:A:G	missense	ENST00000510461.6:c.125T>C	ENSP00000421985.1:p.Ile42Thr
5:131744659:T:C	missense	ENST00000510461.6:c.124A>G	ENSP00000421985.1:p.Ile42Val
5:131744660:C:G	missense	ENST00000510461.6:c.123G>C	ENSP00000421985.1:p.Gln41His
5:131744662:G:A	stop_gain ed	ENST00000510461.6:c.121C>T	ENSP00000421985.1:p.Gln41Ter
5:131744662:G:C	missense	ENST00000510461.6:c.121C>G	ENSP00000421985.1:p.Gln41Glu

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5:131744668:G:T	missense	ENST00000510461.6:c.115C>A	ENSP00000421985.1:p.Pro39Thr
5:131744670:T:G	missense	ENST00000510461.6:c.113A>C	ENSP00000421985.1:p.Asp38Ala
5:131744671:C:G	missense	ENST00000510461.6:c.112G>C	ENSP00000421985.1:p.Asp38His
5:131744671:C:T	missense	ENST00000510461.6:c.112G>A	ENSP00000421985.1:p.Asp38Asn
5:131744673:A:G	missense	ENST00000510461.6:c.110T>C	ENSP00000421985.1:p.Phe37Ser
5:131744675:C:A	missense	ENST00000510461.6:c.108G>T	ENSP00000421985.1:p.Glu36Asp
5:131744676:T:C	missense	ENST00000510461.6:c.107A>G	ENSP00000421985.1:p.Glu36Gly
5:131744676:T:G	missense	ENST00000510461.6:c.107A>C	ENSP00000421985.1:p.Glu36Ala
5:131744677:C:G	missense	ENST00000510461.6:c.106G>C	ENSP00000421985.1:p.Glu36Gln
5:131744679:G:A	missense	ENST00000510461.6:c.104C>T	ENSP00000421985.1:p.Pro35Leu
5:131744680:G:A	missense	ENST00000510461.6:c.103C>T	ENSP00000421985.1:p.Pro35Ser
5:131796828:A:G	splice_donor	ENST00000510461.6:c.92+2T>C	NA
5:131796829:C:T	splice_donor	ENST00000510461.6:c.92+1G>A	NA
5:131796830:C:G	missense	ENST00000510461.6:c.92G>C	ENSP00000421985.1:p.Ser31Thr
5:131796834:A:G	missense	ENST00000510461.6:c.88T>C	ENSP00000421985.1:p.Phe30Leu
5:131796838:G:C	missense	ENST00000510461.6:c.84C>G	ENSP00000421985.1:p.Cys28Trp
5:131796843:C:A	missense	ENST00000510461.6:c.79G>T	ENSP00000421985.1:p.Asp27Tyr

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5:131796843:C:G	missense	ENST00000510461.6:c.79G>C	ENSP00000421985.1:p.Asp27 His
5:131796845:G:A	missense	ENST00000510461.6:c.77C>T	ENSP00000421985.1:p.Pro26L eu
5:131796849:C:A	missense	ENST00000510461.6:c.73G>T	ENSP00000421985.1:p.Asp25T yr
5:131796851:C:G	missense	ENST00000510461.6:c.71G>C	ENSP00000421985.1:p.Arg24P ro
5:131796851:C:T	missense	ENST00000510461.6:c.71G>A	ENSP00000421985.1:p.Arg24G ln
5:131796852:G:A	missense	ENST00000510461.6:c.70C>T	ENSP00000421985.1:p.Arg24T rp
5:131796852:G:C	missense	ENST00000510461.6:c.70C>G	ENSP00000421985.1:p.Arg24G ly
5:131796858:C:A	missense	ENST00000510461.6:c.64G>T	ENSP00000421985.1:p.Asp22T yr
5:131796860:C:T	missense	ENST00000510461.6:c.62G>A	ENSP00000421985.1:p.Arg21H is
5:131796863:C:A	missense	ENST00000510461.6:c.59G>T	ENSP00000421985.1:p.Gly20V al
5:131796863:C:T	missense	ENST00000510461.6:c.59G>A	ENSP00000421985.1:p.Gly20A sp
5:131796866:G:C	missense	ENST00000510461.6:c.56C>G	ENSP00000421985.1:p.Pro19A rg
5:131796867:G:A	missense	ENST00000510461.6:c.55C>T	ENSP00000421985.1:p.Pro19S er
5:131796872:C:A	missense	ENST00000510461.6:c.50G>T	ENSP00000421985.1:p.Gly17V al
5:131796872:C:G	missense	ENST00000510461.6:c.50G>C	ENSP00000421985.1:p.Gly17A la
5:131796875:A:G	missense	ENST00000510461.6:c.47T>C	ENSP00000421985.1:p.Leu16P ro
5:131796878:C:T	missense	ENST00000510461.6:c.44G>A	ENSP00000421985.1:p.Gly15G lu

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5:131796879:C:T	missense	ENST00000510461.6:c.43G>A	ENSP00000421985.1:p.Gly15A rg
5:131796883:C:G	missense	ENST00000510461.6:c.39G>C	ENSP00000421985.1:p.Arg13S er
5:131796884:C:G	missense	ENST00000510461.6:c.38G>C	ENSP00000421985.1:p.Arg13T hr
5:131796887:T:C	missense	ENST00000510461.6:c.35A>G	ENSP00000421985.1:p.Lys12A rg
5:131796889:G:C	missense	ENST00000510461.6:c.33C>G	ENSP00000421985.1:p.Ser11A rg
5:131796891:T:A	missense	ENST00000510461.6:c.31A>T	ENSP00000421985.1:p.Ser11C ys
5:131796897:G:C	missense	ENST00000510461.6:c.25C>G	ENSP00000421985.1:p.Leu9Va l
5:131796899:T:C	missense	ENST00000510461.6:c.23A>G	ENSP00000421985.1:p.Lys8Ar g
5:131796900:T:C	missense	ENST00000510461.6:c.22A>G	ENSP00000421985.1:p.Lys8Gl u
5:131796901:C:G	missense	ENST00000510461.6:c.21G>C	ENSP00000421985.1:p.Gln7Hi s
5:131796904:G:C	missense	ENST00000510461.6:c.18C>G	ENSP00000421985.1:p.Phe6Le u
5:131796906:A:G	missense	ENST00000510461.6:c.16T>C	ENSP00000421985.1:p.Phe6Le u
5:131796911:G:A	missense	ENST00000510461.6:c.11C>T	ENSP00000421985.1:p.Thr4M et
5:131796911:G:T	missense	ENST00000510461.6:c.11C>A	ENSP00000421985.1:p.Thr4Ly s
5:131796912:T:A	missense	ENST00000510461.6:c.10A>T	ENSP00000421985.1:p.Thr4Se r
5:131796914:G:C	missense	ENST00000510461.6:c.8C>G	ENSP00000421985.1:p.Pro3Ar g
5:131796915:G:A	missense	ENST00000510461.6:c.7C>T	ENSP00000421985.1:p.Pro3Se r

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5:131796917:G:A	missense	ENST00000510461.6:c.5C>T	ENSP00000421985.1:p.Ala2Val
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Table 9: Predicted loss of function or deleterious missense variants in FLCN identified by whole exome sequencing

Variant	Effect	hgvs	hgvs
17:17213659:TTC CGAGAC:T	frameshift	ENST00000285071.9:c.1728 _1735del	ENSP00000285071.4:p.Ser577 LeufsTer22
17:17213680:G:T	missense	ENST00000285071.9:c.1715 C>A	ENSP00000285071.4:p.Pro572 His
17:17213686:C:G	missense	ENST00000285071.9:c.1709 G>C	ENSP00000285071.4:p.Arg570 Pro
17:17213686:C:T	missense	ENST00000285071.9:c.1709 G>A	ENSP00000285071.4:p.Arg570 His
17:17213686:CG: C	frameshift	ENST00000285071.9:c.1708 del	ENSP00000285071.4:p.Arg570 AlafsTer18
17:17213687:G:A	missense	ENST00000285071.9:c.1708 C>T	ENSP00000285071.4:p.Arg570 Cys
17:17213695:G:A	missense	ENST00000285071.9:c.1700 C>T	ENSP00000285071.4:p.Ser567 Phe
17:17213703:G:C	missense	ENST00000285071.9:c.1692 C>G	ENSP00000285071.4:p.His564 Gln
17:17213705:G:A	missense	ENST00000285071.9:c.1690 C>T	ENSP00000285071.4:p.His564 Tyr
17:17213705:GT: G	frameshift	ENST00000285071.9:c.1689 del	ENSP00000285071.4:p.His564 ThrfsTer24
17:17213711:T:C	missense	ENST00000285071.9:c.1684 A>G	ENSP00000285071.4:p.Lys562 Glu
17:17213712:G:C	stop_gained	ENST00000285071.9:c.1683 C>G	ENSP00000285071.4:p.Tyr561 Ter
17:17213712:G:T	stop_gained	ENST00000285071.9:c.1683 C>A	ENSP00000285071.4:p.Tyr561 Ter

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17:17213737:C:T	stop_gain d	ENST00000285071.9:c.1658 G>A	ENSP00000285071.4:p.Trp553 Ter
17:17213738:A:G	missense	ENST00000285071.9:c.1657 T>C	ENSP00000285071.4:p.Trp553 Arg
17:17213747:G:C	missense	ENST00000285071.9:c.1648 C>G	ENSP00000285071.4:p.Leu550 Val
17:17213749:A:G	missense	ENST00000285071.9:c.1646 T>C	ENSP00000285071.4:p.Leu549 Pro
17:17213758:T:C	missense	ENST00000285071.9:c.1637 A>G	ENSP00000285071.4:p.Asn546 Ser
17:17213789:G:T	missense	ENST00000285071.9:c.1606 C>A	ENSP00000285071.4:p.Leu536 Met
17:17213796:C:G	missense	ENST00000285071.9:c.1599 G>C	ENSP00000285071.4:p.Gln533 His
17:17213796:CTG :C	frameshift	ENST00000285071.9:c.1597 _1598del	ENSP00000285071.4:p.Gln533 GlufsTer68
17:17213798:G:A	stop_gain d	ENST00000285071.9:c.1597 C>T	ENSP00000285071.4:p.Gln533 Ter
17:17213805:C:G	missense	ENST00000285071.9:c.1590 G>C	ENSP00000285071.4:p.Glu530 Asp
17:17213815:C:C T	frameshift	ENST00000285071.9:c.1579 _1580insA	ENSP00000285071.4:p.Arg527 GlnfsTer75
17:17213815:C:T	missense	ENST00000285071.9:c.1580 G>A	ENSP00000285071.4:p.Arg527 Gln
17:17213816:G:A	stop_gain d	ENST00000285071.9:c.1579 C>T	ENSP00000285071.4:p.Arg527 Ter
17:17213823:C:C A	frameshift	ENST00000285071.9:c.1571 dup	ENSP00000285071.4:p.Asp525 GlyfsTer77
17:17213834:A:C	missense	ENST00000285071.9:c.1561 T>G	ENSP00000285071.4:p.Phe521 Val
17:17213836:T:C	missense	ENST00000285071.9:c.1559 A>G	ENSP00000285071.4:p.Lys520 Arg
17:17213848:T:C	missense	ENST00000285071.9:c.1547 A>G	ENSP00000285071.4:p.Lys516 Arg

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17:17213849:T:C	missense	ENST00000285071.9:c.1546 A>G	ENSP00000285071.4:p.Lys516 Glu
17:17213852:C:T	missense	ENST00000285071.9:c.1543 G>A	ENSP00000285071.4:p.Val515 Met
17:17213855:T:C	missense	ENST00000285071.9:c.1540 A>G	ENSP00000285071.4:p.Lys514 Glu
17:17214984:C:G	splice_don or	ENST00000285071.9:c.1538 +1G>C	NA
17:17214984:C:T	splice_don or	ENST00000285071.9:c.1538 +1G>A	NA
17:17214993:C:G	missense	ENST00000285071.9:c.1530 G>C	ENSP00000285071.4:p.Glu510 Asp
17:17214995:C:T	missense	ENST00000285071.9:c.1528 G>A	ENSP00000285071.4:p.Glu510 Lys
17:17214996:C:A	missense	ENST00000285071.9:c.1527 G>T	ENSP00000285071.4:p.Glu509 Asp
17:17215001:T:A	stop_gaine d	ENST00000285071.9:c.1522 A>T	ENSP00000285071.4:p.Lys508 Ter
17:17215001:T:G	missense	ENST00000285071.9:c.1522 A>C	ENSP00000285071.4:p.Lys508 Gln
17:17215004:G:A	missense	ENST00000285071.9:c.1519 C>T	ENSP00000285071.4:p.Leu507 Phe
17:17215006:C:T	missense	ENST00000285071.9:c.1517 G>A	ENSP00000285071.4:p.Cys506 Tyr
17:17215013:G:A	missense	ENST00000285071.9:c.1510 C>T	ENSP00000285071.4:p.Leu504 Phe
17:17215015:C:T	missense	ENST00000285071.9:c.1508 G>A	ENSP00000285071.4:p.Cys503 Tyr
17:17215016:A:G	missense	ENST00000285071.9:c.1507 T>C	ENSP00000285071.4:p.Cys503 Arg
17:17215022:C:A	missense	ENST00000285071.9:c.1501 G>T	ENSP00000285071.4:p.Asp501 Tyr
17:17215024:A:C	missense	ENST00000285071.9:c.1499 T>G	ENSP00000285071.4:p.Val500 Gly

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17:17215036:G:A	missense	ENST00000285071.9:c.1487 C>T	ENSP00000285071.4:p.Ser496 Phe
17:17215036:G:C	missense	ENST00000285071.9:c.1487 C>G	ENSP00000285071.4:p.Ser496 Cys
17:17215037:A:C	missense	ENST00000285071.9:c.1486 T>G	ENSP00000285071.4:p.Ser496 Ala
17:17215048:T:C	missense	ENST00000285071.9:c.1475 A>G	ENSP00000285071.4:p.Asn492 Ser
17:17215057:G:C	missense	ENST00000285071.9:c.1466 C>G	ENSP00000285071.4:p.Ala489 Gly
17:17215070:T:C	missense	ENST00000285071.9:c.1453 A>G	ENSP00000285071.4:p.Lys485 Glu
17:17215073:T:G	missense	ENST00000285071.9:c.1450 A>C	ENSP00000285071.4:p.Asn484 His
17:17215082:TG: T	frameshift	ENST00000285071.9:c.1440 del	ENSP00000285071.4:p.Thr481 ProfsTer3
17:17215087:C:T	missense	ENST00000285071.9:c.1436 G>A	ENSP00000285071.4:p.Gly479 Asp
17:17215184:C:G	splice_don or	ENST00000285071.9:c.1432 +1G>C	NA
17:17215184:C:T	splice_don or	ENST00000285071.9:c.1432 +1G>A	NA
17:17215188:G:A	stop_gaine d	ENST00000285071.9:c.1429 C>T	ENSP00000285071.4:p.Arg477 Ter
17:17215190:T:T C	frameshift	ENST00000285071.9:c.1426 dup	ENSP00000285071.4:p.Asp476 GlyfsTer10
17:17215224:A:A C	frameshift	ENST00000285071.9:c.1392 dup	ENSP00000285071.4:p.Phe465 ValfsTer21
17:17215228:G:C	stop_gaine d	ENST00000285071.9:c.1389 C>G	ENSP00000285071.4:p.Tyr463 Ter
17:17215236:TGA :T	frameshift	ENST00000285071.9:c.1379 _1380del	ENSP00000285071.4:p.Leu460 GlnfsTer25
17:17215256:CA: C	frameshift	ENST00000285071.9:c.1360 del	ENSP00000285071.4:p.Cys454 ValfsTer14

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17:17215257:AC: A	frameshift	ENST00000285071.9:c.1359 del	ENSP00000285071.4:p.Cys454 ValfsTer14
17:17215263:C:C AGGGTGG	frameshift	ENST00000285071.9:c.1347 _1353dup	ENSP00000285071.4:p.Val452 ProfsTer6
17:17215264:AG GGTGGAGGGTGG AACGTGC:A	frameshift	ENST00000285071.9:c.1333 _1352del	ENSP00000285071.4:p.Ala445 CysfsTer4
17:17215282:T:T GCGGCTGCGTGG ACCTC	frameshift	ENST00000285071.9:c.1318 _1334dup	ENSP00000285071.4:p.Leu449 GlnfsTer25
17:17215302:C:T	missense	ENST00000285071.9:c.1315 G>A	ENSP00000285071.4:p.Val439 Met
17:17215311:CA: C	frameshift	ENST00000285071.9:c.1305 del	ENSP00000285071.4:p.Phe435 LeufsTer33
17:17215313:A:C	missense	ENST00000285071.9:c.1304 T>G	ENSP00000285071.4:p.Phe435 Cys
17:17215317:CTG :C	splice_acce ptor	ENST00000285071.9:c.1301- 3_1301-2del	NA
17:17216382:G:A	missense	ENST00000285071.9:c.1298 C>T	ENSP00000285071.4:p.Ser433 Leu
17:17216394:T:T G	frameshift	ENST00000285071.9:c.1285 dup	ENSP00000285071.4:p.His429 ProfsTer27
17:17216394:TG: T	frameshift	ENST00000285071.9:c.1285 del	ENSP00000285071.4:p.His429 ThrfsTer39
17:17216395:G:T	missense	ENST00000285071.9:c.1285 C>A	ENSP00000285071.4:p.His429 Asn
17:17216400:G:A	missense	ENST00000285071.9:c.1280 C>T	ENSP00000285071.4:p.Pro427 Leu
17:17216400:G:C	missense	ENST00000285071.9:c.1280 C>G	ENSP00000285071.4:p.Pro427 Arg
17:17216400:G:T	missense	ENST00000285071.9:c.1280 C>A	ENSP00000285071.4:p.Pro427 His
17:17216401:G:A	missense	ENST00000285071.9:c.1279 C>T	ENSP00000285071.4:p.Pro427 Ser

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17:17216401:G:T	missense	ENST00000285071.9:c.1279 C>A	ENSP00000285071.4:p.Pro427 Thr
17:17216418:C:A	missense	ENST00000285071.9:c.1262 G>T	ENSP00000285071.4:p.Ser421 Ile
17:17216418:C:C T	frameshift	ENST00000285071.9:c.1261 dup	ENSP00000285071.4:p.Ser421 LysfsTer35
17:17216424:C:A	missense	ENST00000285071.9:c.1256 G>T	ENSP00000285071.4:p.Gly419 Val
17:17216424:C:T	missense	ENST00000285071.9:c.1256 G>A	ENSP00000285071.4:p.Gly419 Glu
17:17216426:C:C A	frameshift	ENST00000285071.9:c.1253 dup	ENSP00000285071.4:p.Leu420 AlafsTer36
17:17216427:AG: A	frameshift	ENST00000285071.9:c.1252 del	ENSP00000285071.4:p.Leu418 TrpfsTer50
17:17216433:T:C	missense	ENST00000285071.9:c.1247 A>G	ENSP00000285071.4:p.Asn416 Ser
17:17216435:G:T	stop_gained	ENST00000285071.9:c.1245 C>A	ENSP00000285071.4:p.Cys415 Ter
17:17216440:G:A	missense	ENST00000285071.9:c.1240 C>T	ENSP00000285071.4:p.Arg414 Trp
17:17216443:A:T	missense	ENST00000285071.9:c.1237 T>A	ENSP00000285071.4:p.Tyr413 Asn
17:17216453:G:C	stop_gained	ENST00000285071.9:c.1227 C>G	ENSP00000285071.4:p.Tyr409 Ter
17:17216454:T:C	missense	ENST00000285071.9:c.1226 A>G	ENSP00000285071.4:p.Tyr409 Cys
17:17216458:G:A	stop_gained	ENST00000285071.9:c.1222 C>T	ENSP00000285071.4:p.Gln408 Ter
17:17216464:T:C	missense	ENST00000285071.9:c.1216 A>G	ENSP00000285071.4:p.Ser406 Gly
17:17216466:T:C	missense	ENST00000285071.9:c.1214 A>G	ENSP00000285071.4:p.Tyr405 Cys
17:17216466:T:T A	frameshift	ENST00000285071.9:c.1213 dup	ENSP00000285071.4:p.Tyr405 LeufsTer51

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17:17216476:T:T G	frameshift	ENST00000285071.9:c.1203 dup	ENSP00000285071.4:p.Ile402H isfsTer54
17:17216478:C:A	missense	ENST00000285071.9:c.1202 G>T	ENSP00000285071.4:p.Arg401 Leu
17:17216479:G:C	missense	ENST00000285071.9:c.1201 C>G	ENSP00000285071.4:p.Arg401 Gly
17:17216482:C:A	missense	ENST00000285071.9:c.1198 G>T	ENSP00000285071.4:p.Val400 Phe
17:17216484:C:A	missense	ENST00000285071.9:c.1196 G>T	ENSP00000285071.4:p.Cys399 Phe
17:17216484:C:T	missense	ENST00000285071.9:c.1196 G>A	ENSP00000285071.4:p.Cys399 Tyr
17:17216485:A:G	missense	ENST00000285071.9:c.1195 T>C	ENSP00000285071.4:p.Cys399 Arg
17:17216487:C:G	missense	ENST00000285071.9:c.1193 G>C	ENSP00000285071.4:p.Gly398 Ala
17:17216491:C:C G	frameshift	ENST00000285071.9:c.1188 dup	ENSP00000285071.4:p.Val397 ArgfsTer59
17:17217068:C:G	splice_don or	ENST00000285071.9:c.1176 +1G>C	NA
17:17217068:CCC GAAGTACTTCAAA AGCTGACT:C	frameshift	ENST00000285071.9:c.1154 _1176del	ENSP00000285071.4:p.Gln385 HisfsTer63
17:17217074:G:T	missense	ENST00000285071.9:c.1171 C>A	ENSP00000285071.4:p.Leu391 Ile
17:17217086:C:G	missense	ENST00000285071.9:c.1159 G>C	ENSP00000285071.4:p.Ala387 Pro
17:17217092:G:A	stop_gaine d	ENST00000285071.9:c.1153 C>T	ENSP00000285071.4:p.Gln385 Ter
17:17217112:C:C T	frameshift	ENST00000285071.9:c.1132 dup	ENSP00000285071.4:p.Ser378 LysfsTer12
17:17217116:TC: T	frameshift	ENST00000285071.9:c.1128 del	ENSP00000285071.4:p.Trp376 Ter

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17:17217124:A:T	missense	ENST00000285071.9:c.1121 T>A	ENSP00000285071.4:p.Val374 Glu
17:17217127:TG: T	frameshift	ENST00000285071.9:c.1117 del	ENSP00000285071.4:p.Gln373 ArgfsTer2
17:17217128:G:A	stop_gained	ENST00000285071.9:c.1117 C>T	ENSP00000285071.4:p.Gln373 Ter
17:17217133:C:T	missense	ENST00000285071.9:c.1112 G>A	ENSP00000285071.4:p.Gly371 Glu
17:17217147:C:T	stop_gained	ENST00000285071.9:c.1098 G>A	ENSP00000285071.4:p.Trp366 Ter
17:17217161:G:A	missense	ENST00000285071.9:c.1084 C>T	ENSP00000285071.4:p.Arg362 Cys
17:17217163:A:G	missense	ENST00000285071.9:c.1082 T>C	ENSP00000285071.4:p.Phe361 Ser
17:17217168:AG: A	frameshift	ENST00000285071.9:c.1076 del	ENSP00000285071.4:p.Pro359 LeufsTer16
17:17217174:AC: A	frameshift	ENST00000285071.9:c.1070 del	ENSP00000285071.4:p.Gly357 ValfsTer18
17:17217175:C:A	missense	ENST00000285071.9:c.1070 G>T	ENSP00000285071.4:p.Gly357 Val
17:17217183:C:A	splice_acceptor	ENST00000285071.9:c.1063- 1G>T	NA
17:17217184:T:A	splice_acceptor	ENST00000285071.9:c.1063- 2A>T	NA
17:17217184:T:C	splice_acceptor	ENST00000285071.9:c.1063- 2A>G	NA
17:17219017:A:C	splice_donor	ENST00000285071.9:c.1062 +2T>G	NA
17:17219018:C:T	splice_donor	ENST00000285071.9:c.1062 +1G>A	NA
17:17219030:G:A	missense	ENST00000285071.9:c.1051 C>T	ENSP00000285071.4:p.His351 Tyr
17:17219032:C:T	missense	ENST00000285071.9:c.1049 G>A	ENSP00000285071.4:p.Arg350 Gln

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17:17219033:G:A	missense	ENST00000285071.9:c.1048 C>T	ENSP00000285071.4:p.Arg350 Trp
17:17219038:G:A	missense	ENST00000285071.9:c.1043 C>T	ENSP00000285071.4:p.Ser348 Phe
17:17219038:G:T	missense	ENST00000285071.9:c.1043 C>A	ENSP00000285071.4:p.Ser348 Tyr
17:17219051:G:G CAGATTCCGGGG CTGC	frameshift	ENST00000285071.9:c.1029 _1030insGCAGCCCCGGAATC TG	ENSP00000285071.4:p.Pro344 AlafsTer51
17:17219082:TGA GA:T	frameshift	ENST00000285071.9:c.995_ 998del	ENSP00000285071.4:p.Leu332 GlnfsTer20
17:17219126:C:C TTCTGTACTCTCT GGCAACACAGGG GCT	frameshift	ENST00000285071.9:c.927_ 954dup	ENSP00000285071.4:p.Gly319 SerfsTer80
17:17219133:ACT :A	frameshift	ENST00000285071.9:c.946_ 947del	ENSP00000285071.4:p.Ser316 TyrfsTer73
17:17219147:CAG :C	frameshift	ENST00000285071.9:c.932_ 933del	ENSP00000285071.4:p.Pro311 ArgfsTer78
17:17219148:A:A G	frameshift	ENST00000285071.9:c.932d up	ENSP00000285071.4:p.Val312 CysfsTer78
17:17219174:C:C A	frameshift	ENST00000285071.9:c.906d up	ENSP00000285071.4:p.Glu303 Ter
17:17219176:G:C	missense	ENST00000285071.9:c.905C >G	ENSP00000285071.4:p.Ser302 Cys
17:17219177:A:G	missense	ENST00000285071.9:c.904T >C	ENSP00000285071.4:p.Ser302 Pro
17:17219183:C:G	missense	ENST00000285071.9:c.898G >C	ENSP00000285071.4:p.Asp300 His
17:17219187:GCT TT:G	frameshift	ENST00000285071.9:c.890_ 893del	ENSP00000285071.4:p.Glu297 AlafsTer25
17:17219190:TTC :T	frameshift	ENST00000285071.9:c.889_ 890del	ENSP00000285071.4:p.Glu297 LysfsTer6

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17:17219194:G:C	stop_gain d	ENST00000285071.9:c.887C >G	ENSP00000285071.4:p.Ser296 Ter
17:17219194:G:T	stop_gain d	ENST00000285071.9:c.887C >A	ENSP00000285071.4:p.Ser296 Ter
17:17219201:C:G	missense	ENST00000285071.9:c.880G >C	ENSP00000285071.4:p.Glu294 Gln
17:17219206:A:C	stop_gain d	ENST00000285071.9:c.875T >G	ENSP00000285071.4:p.Leu292 Ter
17:17221535:A:G	splice_don or	ENST00000285071.9:c.871+ 2T>C	NA
17:17221549:C:T	missense	ENST00000285071.9:c.859G >A	ENSP00000285071.4:p.Glu287 Lys
17:17221555:G:A	stop_gain d	ENST00000285071.9:c.853C >T	ENSP00000285071.4:p.Gln285 Ter
17:17221567:C:A	missense	ENST00000285071.9:c.841G >T	ENSP00000285071.4:p.Asp281 Tyr
17:17221570:C:T	missense	ENST00000285071.9:c.838G >A	ENSP00000285071.4:p.Glu280 Lys
17:17221575:G:A	missense	ENST00000285071.9:c.833C >T	ENSP00000285071.4:p.Pro278 Leu
17:17221576:G:C	missense	ENST00000285071.9:c.832C >G	ENSP00000285071.4:p.Pro278 Ala
17:17221597:C:T	missense	ENST00000285071.9:c.811G >A	ENSP00000285071.4:p.Glu271 Lys
17:17221599:G:A	missense	ENST00000285071.9:c.809C >T	ENSP00000285071.4:p.Thr270 Ile
17:17221605:C:T	missense	ENST00000285071.9:c.803G >A	ENSP00000285071.4:p.Arg268 Gln
17:17221612:C:T	missense	ENST00000285071.9:c.796G >A	ENSP00000285071.4:p.Gly266 Ser
17:17221614:C:T	missense	ENST00000285071.9:c.794G >A	ENSP00000285071.4:p.Cys265 Tyr
17:17221617:G:A	missense	ENST00000285071.9:c.791C >T	ENSP00000285071.4:p.Ala264 Val

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17:17221617:G:C	missense	ENST00000285071.9:c.791C >G	ENSP00000285071.4:p.Ala264 Gly
17:17221618:C:A	missense	ENST00000285071.9:c.790G >T	ENSP00000285071.4:p.Ala264 Ser
17:17221618:C:G	missense	ENST00000285071.9:c.790G >C	ENSP00000285071.4:p.Ala264 Pro
17:17221627:G:A	missense	ENST00000285071.9:c.781C >T	ENSP00000285071.4:p.Leu261 Phe
17:17221628:C:T	stop_gained	ENST00000285071.9:c.780G >A	ENSP00000285071.4:p.Trp260 Ter
17:17221630:T:C	splice_acceptor	ENST00000285071.9:c.780- 2A>G	NA
17:17222500:C:A	splice_donor	ENST00000285071.9:c.779+ 1G>T	NA
17:17222501:C:G	missense	ENST00000285071.9:c.779G >C	ENSP00000285071.4:p.Trp260 Ser
17:17222516:T:G	missense	ENST00000285071.9:c.764A >C	ENSP00000285071.4:p.His255 Pro
17:17222517:G:A	missense	ENST00000285071.9:c.763C >T	ENSP00000285071.4:p.His255 Tyr
17:17222519:A:G	missense	ENST00000285071.9:c.761T >C	ENSP00000285071.4:p.Leu254 Pro
17:17222525:G:G C	frameshift	ENST00000285071.9:c.754d up	ENSP00000285071.4:p.Ala252 GlyfsTer40
17:17222532:G:T	missense	ENST00000285071.9:c.748C >A	ENSP00000285071.4:p.Leu250 Met
17:17222540:T:C	missense	ENST00000285071.9:c.740A >G	ENSP00000285071.4:p.Asp247 Gly
17:17222541:CAC TT:C	frameshift	ENST00000285071.9:c.735_ 738del	ENSP00000285071.4:p.Ser246 MetfsTer16
17:17222546:G:T	missense	ENST00000285071.9:c.734C >A	ENSP00000285071.4:p.Thr245 Lys
17:17222558:A:C	missense	ENST00000285071.9:c.722T >G	ENSP00000285071.4:p.Leu241 Arg

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17:17222558:A:G	missense	ENST00000285071.9:c.722T >C	ENSP00000285071.4:p.Leu241 Pro
17:17222559:G:C	missense	ENST00000285071.9:c.721C >G	ENSP00000285071.4:p.Leu241 Val
17:17222561:G:A	missense	ENST00000285071.9:c.719C >T	ENSP00000285071.4:p.Ser240 Leu
17:17222564:C:T	missense	ENST00000285071.9:c.716G >A	ENSP00000285071.4:p.Arg239 His
17:17222565:G:A	missense	ENST00000285071.9:c.715C >T	ENSP00000285071.4:p.Arg239 Cys
17:17222565:G:C	missense	ENST00000285071.9:c.715C >G	ENSP00000285071.4:p.Arg239 Gly
17:17222582:C:T	missense	ENST00000285071.9:c.698G >A	ENSP00000285071.4:p.Arg233 Lys
17:17222590:T:T A	frameshift	ENST00000285071.9:c.689d up	ENSP00000285071.4:p.His231 ThrfsTer17
17:17222615:A:C	missense	ENST00000285071.9:c.665T >G	ENSP00000285071.4:p.Met22 2Arg
17:17222618:C:A	missense	ENST00000285071.9:c.662G >T	ENSP00000285071.4:p.Arg221 Met
17:17222628:G:A	missense	ENST00000285071.9:c.652C >T	ENSP00000285071.4:p.Arg218 Cys
17:17222632:TG: T	frameshift	ENST00000285071.9:c.647d el	ENSP00000285071.4:p.Pro216 HisfsTer7
17:17222636:C:T	missense	ENST00000285071.9:c.644G >A	ENSP00000285071.4:p.Cys215 Tyr
17:17222649:C:T	missense	ENST00000285071.9:c.631G >A	ENSP00000285071.4:p.Glu211 Lys
17:17222657:A:C	missense	ENST00000285071.9:c.623T >G	ENSP00000285071.4:p.Phe208 Cys
17:17222662:C:T	splice_acce ptor	ENST00000285071.9:c.619- 1G>A	NA
17:17222663:T:G	splice_acce ptor	ENST00000285071.9:c.619- 2A>C	NA

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17:17223929:G:A	missense	ENST00000285071.9:c.611C >T	ENSP00000285071.4:p.Ala204 Val
17:17223930:C:T	missense	ENST00000285071.9:c.610G >A	ENSP00000285071.4:p.Ala204 Thr
17:17223937:C:A	missense	ENST00000285071.9:c.603G >T	ENSP00000285071.4:p.Gln201 His
17:17223937:C:G	missense	ENST00000285071.9:c.603G >C	ENSP00000285071.4:p.Gln201 His
17:17223942:G:A	missense	ENST00000285071.9:c.598C >T	ENSP00000285071.4:p.Leu200 Phe
17:17223951:T:A	missense	ENST00000285071.9:c.589A >T	ENSP00000285071.4:p.Ile197P he
17:17223955:TC: T	frameshift	ENST00000285071.9:c.584d el	ENSP00000285071.4:p.Gly195 GlufsTer28
17:17223959:C:A	missense	ENST00000285071.9:c.581G >T	ENSP00000285071.4:p.Arg194 Leu
17:17223960:G:A	missense	ENST00000285071.9:c.580C >T	ENSP00000285071.4:p.Arg194 Trp
17:17223966:T:A	stop_gaine d	ENST00000285071.9:c.574A >T	ENSP00000285071.4:p.Lys192 Ter
17:17223975:G:C	missense	ENST00000285071.9:c.565C >G	ENSP00000285071.4:p.Leu189 Val
17:17223978:A:T	missense	ENST00000285071.9:c.562T >A	ENSP00000285071.4:p.Phe188 Ile
17:17223980:G:A	missense	ENST00000285071.9:c.560C >T	ENSP00000285071.4:p.Pro187 Leu
17:17223981:G:T	missense	ENST00000285071.9:c.559C >A	ENSP00000285071.4:p.Pro187 Thr
17:17223983:C:A	missense	ENST00000285071.9:c.557G >T	ENSP00000285071.4:p.Trp186 Leu
17:17223986:G:A	missense	ENST00000285071.9:c.554C >T	ENSP00000285071.4:p.Ser185 Phe
17:17223989:T:G	missense	ENST00000285071.9:c.551A >C	ENSP00000285071.4:p.Asn184 Thr

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17:17223995:A:G	missense	ENST00000285071.9:c.545T >C	ENSP00000285071.4:p.Leu182 Pro
17:17223996:G:A	missense	ENST00000285071.9:c.544C >T	ENSP00000285071.4:p.Leu182 Phe
17:17223998:T:C	missense	ENST00000285071.9:c.542A >G	ENSP00000285071.4:p.Tyr181 Cys
17:17224001:A:G	missense	ENST00000285071.9:c.539T >C	ENSP00000285071.4:p.Ile180T hr
17:17224001:A:T	missense	ENST00000285071.9:c.539T >A	ENSP00000285071.4:p.Ile180A sn
17:17224002:T:A	missense	ENST00000285071.9:c.538A >T	ENSP00000285071.4:p.Ile180P he
17:17224004:C:T	missense	ENST00000285071.9:c.536G >A	ENSP00000285071.4:p.Arg179 Gln
17:17224005:G:A	missense	ENST00000285071.9:c.535C >T	ENSP00000285071.4:p.Arg179 Trp
17:17224008:C:A	missense	ENST00000285071.9:c.532G >T	ENSP00000285071.4:p.Asp178 Tyr
17:17224012:CAT GATGG:C	frameshift	ENST00000285071.9:c.521_ 527del	ENSP00000285071.4:p.Thr174 ArgfsTer47
17:17224017:T:A	missense	ENST00000285071.9:c.523A >T	ENSP00000285071.4:p.Ile175P he
17:17224021:G:C	missense	ENST00000285071.9:c.519C >G	ENSP00000285071.4:p.Ile173 Met
17:17224030:G:T	stop_gained	ENST00000285071.9:c.510C >A	ENSP00000285071.4:p.Tyr170 Ter
17:17224032:A:G	missense	ENST00000285071.9:c.508T >C	ENSP00000285071.4:p.Tyr170 His
17:17224032:A:T	missense	ENST00000285071.9:c.508T >A	ENSP00000285071.4:p.Tyr170 Asn
17:17224035:A:G	missense	ENST00000285071.9:c.505T >C	ENSP00000285071.4:p.Trp169 Arg
17:17224037:C:T	missense	ENST00000285071.9:c.503G >A	ENSP00000285071.4:p.Arg168 His

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17:17224038:G:A	missense	ENST00000285071.9:c.502C >T	ENSP00000285071.4:p.Arg168 Cys
17:17224039:C:G	missense	ENST00000285071.9:c.501G >C	ENSP00000285071.4:p.Gln167 His
17:17224041:G:A	stop_gained	ENST00000285071.9:c.499C >T	ENSP00000285071.4:p.Gln167 Ter
17:17224053:C:A	missense	ENST00000285071.9:c.487G >T	ENSP00000285071.4:p.Ala163 Ser
17:17224062:C:A	missense	ENST00000285071.9:c.478G >T	ENSP00000285071.4:p.Asp160 Tyr
17:17224073:A:G	missense	ENST00000285071.9:c.467T >C	ENSP00000285071.4:p.Phe156 Ser
17:17224076:G:T	missense	ENST00000285071.9:c.464C >A	ENSP00000285071.4:p.Thr155 Asn
17:17224077:T:A	missense	ENST00000285071.9:c.463A >T	ENSP00000285071.4:p.Thr155 Ser
17:17224083:T:C	missense	ENST00000285071.9:c.457A >G	ENSP00000285071.4:p.Ser153 Gly
17:17224088:A:G	missense	ENST00000285071.9:c.452T >C	ENSP00000285071.4:p.Val151 Ala
17:17224089:C:T	missense	ENST00000285071.9:c.451G >A	ENSP00000285071.4:p.Val151 Met
17:17224091:A:G	missense	ENST00000285071.9:c.449T >C	ENSP00000285071.4:p.Phe150 Ser
17:17224092:A:C	missense	ENST00000285071.9:c.448T >G	ENSP00000285071.4:p.Phe150 Val
17:17224095:C:T	missense	ENST00000285071.9:c.445G >A	ENSP00000285071.4:p.Gly149 Ser
17:17224099:C:C TG	frameshift	ENST00000285071.9:c.439_ 440dup	ENSP00000285071.4:p.Gln147 HisfsTer31
17:17224099:CT: C	frameshift	ENST00000285071.9:c.440d el	ENSP00000285071.4:p.Gln147 ArgfsTer30
17:17224104:C:T	missense	ENST00000285071.9:c.436G >A	ENSP00000285071.4:p.Glu146 Lys

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17:17224107:C:T	missense	ENST00000285071.9:c.433G >A	ENSP00000285071.4:p.Asp145 Asn
17:17224110:C:T	missense	ENST00000285071.9:c.430G >A	ENSP00000285071.4:p.Gly144 Arg
17:17224111:G:C	missense	ENST00000285071.9:c.429C >G	ENSP00000285071.4:p.Phe143 Leu
17:17224111:G:T	missense	ENST00000285071.9:c.429C >A	ENSP00000285071.4:p.Phe143 Leu
17:17224115:A:C	missense	ENST00000285071.9:c.425T >G	ENSP00000285071.4:p.Phe142 Cys
17:17224121:G:A	missense	ENST00000285071.9:c.419C >T	ENSP00000285071.4:p.Pro140 Leu
17:17224121:G:C	missense	ENST00000285071.9:c.419C >G	ENSP00000285071.4:p.Pro140 Arg
17:17224124:C:A	missense	ENST00000285071.9:c.416G >T	ENSP00000285071.4:p.Gly139 Val
17:17224125:C:T	missense	ENST00000285071.9:c.415G >A	ENSP00000285071.4:p.Gly139 Ser
17:17224128:C:T	missense	ENST00000285071.9:c.412G >A	ENSP00000285071.4:p.Glu138 Lys
17:17224130:C:A	missense	ENST00000285071.9:c.410G >T	ENSP00000285071.4:p.Arg137 Leu
17:17224130:C:T	missense	ENST00000285071.9:c.410G >A	ENSP00000285071.4:p.Arg137 His
17:17224131:G:A	missense	ENST00000285071.9:c.409C >T	ENSP00000285071.4:p.Arg137 Cys
17:17224136:G:A	missense	ENST00000285071.9:c.404C >T	ENSP00000285071.4:p.Pro135 Leu
17:17224136:G:C	missense	ENST00000285071.9:c.404C >G	ENSP00000285071.4:p.Pro135 Arg
17:17224137:G:T	missense	ENST00000285071.9:c.403C >A	ENSP00000285071.4:p.Pro135 Thr
17:17224143:C:A	missense	ENST00000285071.9:c.397G >T	ENSP00000285071.4:p.Val133 Phe

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17:17224143:C:T	missense	ENST00000285071.9:c.397G >A	ENSP00000285071.4:p.Val133I le
17:17226174:A:C	splice_donor	ENST00000285071.9:c.396+ 2T>G	NA
17:17226186:A:C	missense	ENST00000285071.9:c.386T >G	ENSP00000285071.4:p.Leu129 Arg
17:17226187:G:C	missense	ENST00000285071.9:c.385C >G	ENSP00000285071.4:p.Leu129 Val
17:17226192:C:T	missense	ENST00000285071.9:c.380G >A	ENSP00000285071.4:p.Arg127 Gln
17:17226193:G:A	missense	ENST00000285071.9:c.379C >T	ENSP00000285071.4:p.Arg127 Trp
17:17226193:G:C	missense	ENST00000285071.9:c.379C >G	ENSP00000285071.4:p.Arg127 Gly
17:17226202:C:T	missense	ENST00000285071.9:c.370G >A	ENSP00000285071.4:p.Ala124 Thr
17:17226207:C:G	missense	ENST00000285071.9:c.365G >C	ENSP00000285071.4:p.Arg122 Pro
17:17226208:G:A	missense	ENST00000285071.9:c.364C >T	ENSP00000285071.4:p.Arg122 Cys
17:17226210:A:G	missense	ENST00000285071.9:c.362T >C	ENSP00000285071.4:p.Val121 Ala
17:17226220:A:C	missense	ENST00000285071.9:c.352T >G	ENSP00000285071.4:p.Phe118 Val
17:17226224:C:C T	frameshift	ENST00000285071.9:c.347d up	ENSP00000285071.4:p.Leu117 AlafsTer16
17:17226224:C:G	missense	ENST00000285071.9:c.348G >C	ENSP00000285071.4:p.Gln116 His
17:17226243:T:A	missense	ENST00000285071.9:c.329A >T	ENSP00000285071.4:p.Gln110 Leu
17:17226245:G:G T	frameshift	ENST00000285071.9:c.326d up	ENSP00000285071.4:p.His109 GlnfsTer24
17:17226247:G:A	missense	ENST00000285071.9:c.325C >T	ENSP00000285071.4:p.His109 Tyr

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17:17226250:T:T G	frameshift	ENST00000285071.9:c.321d up	ENSP00000285071.4:p.Ser108 GlnfsTer25
17:17226252:A:T	missense	ENST00000285071.9:c.320T >A	ENSP00000285071.4:p.Val107 Asp
17:17226262:T:C	missense	ENST00000285071.9:c.310A >G	ENSP00000285071.4:p.Ile104V al
17:17226270:T:C	missense	ENST00000285071.9:c.302A >G	ENSP00000285071.4:p.Glu101 Gly
17:17226274:T:A	stop_gained	ENST00000285071.9:c.298A >T	ENSP00000285071.4:p.Lys100 Ter
17:17226276:T:C	missense	ENST00000285071.9:c.296A >G	ENSP00000285071.4:p.Asp99 Gly
17:17226277:C:G	missense	ENST00000285071.9:c.295G >C	ENSP00000285071.4:p.Asp99 His
17:17226282:C:T	missense	ENST00000285071.9:c.290G >A	ENSP00000285071.4:p.Ser97A sn
17:17226291:C:G	missense	ENST00000285071.9:c.281G >C	ENSP00000285071.4:p.Gly94A la
17:17226294:G:A	missense	ENST00000285071.9:c.278C >T	ENSP00000285071.4:p.Pro93L eu
17:17226294:G:C	missense	ENST00000285071.9:c.278C >G	ENSP00000285071.4:p.Pro93A rg
17:17226295:G:C	missense	ENST00000285071.9:c.277C >G	ENSP00000285071.4:p.Pro93A la
17:17226297:T:G	missense	ENST00000285071.9:c.275A >C	ENSP00000285071.4:p.His92Pr o
17:17226298:G:A	missense	ENST00000285071.9:c.274C >T	ENSP00000285071.4:p.His92T yr
17:17226301:C:T	missense	ENST00000285071.9:c.271G >A	ENSP00000285071.4:p.Gly91A rg
17:17226315:C:T	missense	ENST00000285071.9:c.257G >A	ENSP00000285071.4:p.Arg86G ln
17:17226316:G:A	missense	ENST00000285071.9:c.256C >T	ENSP00000285071.4:p.Arg86T rp

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17:17226318:C:T	missense	ENST00000285071.9:c.254G >A	ENSP00000285071.4:p.Cys85T yr
17:17226321:C:A	missense	ENST00000285071.9:c.251G >T	ENSP00000285071.4:p.Gly84V al
17:17226324:T:C	splice_acceptor	ENST00000285071.9:c.250- 2A>G	NA
17:17227887:G:A	splice_donor	ENST00000285071.9:c.249+ 2C>T	NA
17:17227887:G:T	splice_donor	ENST00000285071.9:c.249+ 2C>A	NA
17:17227893:C:T	missense	ENST00000285071.9:c.245G >A	ENSP00000285071.4:p.Cys82T yr
17:17227899:TCC GA:T	frameshift	ENST00000285071.9:c.235_ 238del	ENSP00000285071.4:p.Ser79T hrfsTer50
17:17227904:CT: C	frameshift	ENST00000285071.9:c.233d el	ENSP00000285071.4:p.Lys78S erfsTer52
17:17227923:CT: C	frameshift	ENST00000285071.9:c.214d el	ENSP00000285071.4:p.Ser72A lafsTer58
17:17227930:C:A	stop_gained	ENST00000285071.9:c.208G >T	ENSP00000285071.4:p.Glu70T er
17:17227948:CG: C	frameshift	ENST00000285071.9:c.189d el	ENSP00000285071.4:p.Ala64G lnfsTer66
17:17227950:G:T	missense	ENST00000285071.9:c.188C >A	ENSP00000285071.4:p.Pro63H is
17:17227979:CT: C	frameshift	ENST00000285071.9:c.158d el	ENSP00000285071.4:p.Gln53A rgfsTer2
17:17228025:C:C T	frameshift	ENST00000285071.9:c.112d up	ENSP00000285071.4:p.Ser38L ysfsTer6
17:17228040:TC: T	frameshift	ENST00000285071.9:c.97del	ENSP00000285071.4:p.Asp33 MetfsTer22
17:17228073:G:A	missense	ENST00000285071.9:c.65C> T	ENSP00000285071.4:p.Thr22 Met
17:17228077:A:G	missense	ENST00000285071.9:c.61T> C	ENSP00000285071.4:p.Cys21A rg

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17:17228079:A:T	missense	ENST00000285071.9:c.59T> A	ENSP00000285071.4:p.Phe20T yr
17:17228082:A:G	missense	ENST00000285071.9:c.56T> C	ENSP00000285071.4:p.Leu19P ro
17:17228085:G:T	missense	ENST00000285071.9:c.53C> A	ENSP00000285071.4:p.Thr18A sn
17:17228088:C:A	missense	ENST00000285071.9:c.50G> T	ENSP00000285071.4:p.Arg17L eu
17:17228088:C:T	missense	ENST00000285071.9:c.50G> A	ENSP00000285071.4:p.Arg17H is
17:17228089:G:A	missense	ENST00000285071.9:c.49C> T	ENSP00000285071.4:p.Arg17C ys
17:17228091:G:A	missense	ENST00000285071.9:c.47C> T	ENSP00000285071.4:p.Pro16L eu
17:17228095:C:T	missense	ENST00000285071.9:c.43G> A	ENSP00000285071.4:p.Gly15S er
17:17228104:C:G	missense	ENST00000285071.9:c.34G> C	ENSP00000285071.4:p.Glu12G ln
17:17228104:C:T	missense	ENST00000285071.9:c.34G> A	ENSP00000285071.4:p.Glu12L ys
17:17228105:G:C	missense	ENST00000285071.9:c.33C> G	ENSP00000285071.4:p.Cys11T rp
17:17228105:G:T	stop_gained	ENST00000285071.9:c.33C> A	ENSP00000285071.4:p.Cys11T er
17:17228109:A:T	missense	ENST00000285071.9:c.29T> A	ENSP00000285071.4:p.Phe10T yr
17:17228112:T:C	missense	ENST00000285071.9:c.26A> G	ENSP00000285071.4:p.His9Ar g
17:17228114:G:T	stop_gained	ENST00000285071.9:c.24C> A	ENSP00000285071.4:p.Cys8Te r
17:17228115:C:T	missense	ENST00000285071.9:c.23G> A	ENSP00000285071.4:p.Cys8Ty r
17:17228119:G:C	missense	ENST00000285071.9:c.19C> G	ENSP00000285071.4:p.Leu7Va l

17:17228124:A:C	missense	ENST00000285071.9:c.14T>G	ENSP00000285071.4:p.Val5Gly
17:17228133:T:C	missense	ENST00000285071.9:c.5A>G	ENSP00000285071.4:p.Asn2Ser
17:17228136:A:G	start_lost	ENST00000285071.9:c.2T>C	ENSP00000285071.4:p.Met1?
17:17228137:T:C	start_lost	ENST00000285071.9:c.1A>G	ENSP00000285071.4:p.Met1?

Additional data is shown in Figures 1-18.

Figure 1 shows identification of FNIP1 rare coding variation associated with blood lipids and liver enzymes in ExWAS; the largest effect was observed with lower triglycerides and ALT.

Figure 2 shows identification of genome-wide association analysis with a common missense (5:131672501:T:C--Gln648Arg) variant in FNIP1 to be associated with TGL:HDL ratio.

Figure 3 shows association of FNIP1 rare coding variants with higher HDLC and lower triglycerides and LDLC levels; FLCN shows similar pattern of associations.

Figure 4 shows association of FNIP1 and FLCN rare coding variants with lower ALT levels; FLCN pLoFs are associated with lower MRI derived liver fat and inflammation.

Figure 5 shows the impact of FNIP1 and FLCN rare coding variants on ALT and PDFF.

Figure 6 shows association of FNIP1 rare coding variants with lower odds for NALD.

Figure 7 shows association of common FNIP1 missense variant with liver enzymes.

Figure 8 shows association of FNIP1 and FLCN rare coding variants with lower waist to hip ratio and body fat percentage.

Figure 9 shows the impact of rare variation in FNIP1 on body fat distribution.

Figure 10 shows association of FNIP1 and FLCN rare coding variants with lower HbA1c levels and lower odds of type 2 diabetes.

Figure 11 shows association of FNIP1 and FLCN rare coding variants with lower eGFR.

Figure 12 shows FNIP1 pLoF had general protective cardiometabolic associations.

Figure 13 shows FNIP1 pLoF had general protective cardiometabolic associations.

Figure 14 shows FNIP1 common missense variant phenome-wide associations are similar to FNIP1 rare coding associations.

Figure 15 shows FNIP1 common missense variant shows strongest association with lower odds for T2D.

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Example 3: FNIP1 or FLCN Knockdown Effects in Skeletal Muscles

In this example, intramuscular delivery of FNIP1 or FLCN gRNAs was produced through AAV-myo2A vector by pooling multiple gRNAs at the same time to achieve efficient gene perturbation, followed by observation of their knockdown effect on muscle fiber switches, and various mitochondrial gene expression patterns.

Figure 16 shows FNIP1 inhibition in skeletal muscle induced an increase in oxidative muscle fibers and mitochondrial gene expression. Pools of FNIP1 gRNAs were co-packaged into AAVmyo2A, which was obtained from SignaGen Laboratories (Catalog # SL100862). The AAV-gRNA pools were then delivered to Cas9 male mice via intramuscular injection at a dose of 1.5E11 vg per tibialis anterior (TA) muscle, which leads to efficient gene perturbations in TA and extensor digitorum longus (EDL) muscles. At 6 weeks after AAV administration, the following phenotype was observed: a conversion of glycolytic muscle fibers to oxidative muscle fibers with increased expression of mitochondrial genes in TA and EDL muscle. The data are consistent with literature on muscle-specific FNIP1 cKO mice.

Figure 17 shows FNIP1 inhibition in skeletal muscle enhanced vascularization and muscle glycogen content, and increased the expression of genes related to glucose and fatty acid uptake and metabolism. These results suggest: a) FNIP1 gRNAs increase muscle vascularity and enhance nutrient uptake in muscle, consistent with the oxidative myofiber phenotype; and b) skeletal muscle-specific targeting of FNIP1 in adult individuals induces exercise-mimetic effects, which may in part explain the beneficial human genetics associations for FNIP1 pLOF variants: lower HbA1c and T2D risk, lower plasma lipids, and reduced adiposity.

Figure 18 shows FLCN inhibition in skeletal muscle induced an increase in oxidative muscle fibers, enhanced vascularity, and increased glycogen content. Pools of FLCN gRNAs were co-packaged into AAVmyo2A, which was obtained from SignaGen Laboratories (Catalog # SL100862). The AAV-gRNA pools were then delivered to Cas9 male mice via intramuscular injection at a dose of 1.5E11 vg per tibialis anterior (TA) muscle. At 6 weeks after AAV administration, the following phenotype was observed: a conversion of glycolytic muscle fibers to oxidative muscle fibers with increased muscle capillary density and glycogen storage in TA muscle. The data are consistent with literature on muscle-specific FLCN cKO mice, and may in part explain the beneficial human genetics associations for FLCN pLOF variants: lower HbA1c and T2D risk, lower plasma lipids, and reduced adiposity.

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Various modifications of the described subject matter, in addition to those described herein, will be apparent to those skilled in the art from the foregoing description. Such modifications are also intended to fall within the scope of the appended claims. Each reference (including, but not limited to, journal articles, U.S. and non-U.S. patents, patent application
5 publications, international patent application publications, gene bank accession numbers, and the like) cited in the present application is incorporated herein by reference in its entirety and for all purposes.

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What is Claimed is:

1. A method of treating a subject having muscle disorder or at risk of developing muscle disorder, the method comprising administering a Folliculin Interacting Protein 1 (FNIP1) inhibitor and/or a Folliculin (FLCN) inhibitor to the subject.
- 5 2. The method of claim 1, wherein the muscle disorder comprises sarcopenia, Duchenne Muscular Dystrophy, or Pompe disease.
3. The method of claim 1 or claim 2, wherein the FNIP1 inhibitor comprises an inhibitory nucleic acid molecule that hybridizes to an FNIP1 nucleic acid molecule.
4. The method of claim 3, wherein the inhibitory nucleic acid molecule comprises an
10 antisense nucleic acid molecule, a small interfering RNA (siRNA), and/or a short hairpin RNA (shRNA).
5. The method of claim 4, wherein the inhibitory nucleic acid molecule comprises an siRNA.
6. The method of claim 4, wherein the inhibitory nucleic acid molecule comprises an
15 antisense nucleic acid molecule.
7. The method of any one of claims 1 to 6, wherein the FLCN inhibitor comprises an inhibitory nucleic acid molecule that hybridizes to an FLCN nucleic acid molecule.
8. The method of claim 7, wherein the inhibitory nucleic acid molecule comprises an
antisense nucleic acid molecule, a small interfering RNA (siRNA), and/or a short hairpin RNA
20 (shRNA).
9. The method of claim 8, wherein the inhibitory nucleic acid molecule comprises an siRNA.
10. The method of claim 8, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule.
- 25 11. The method of any one of claims 1 to 10, wherein the subject is also administered a muscle disorder therapeutic agent.
12. The method of any one of claims 1 to 11, further comprising detecting the presence or absence of an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule in a biological sample from the subject.
- 30 13. The method of claim 12, comprising administering a muscle disorder therapeutic agent in a standard dosage amount to the subject when the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule is absent from the biological sample.

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14. The method of claim 12, further comprising administering a muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount to the subject when the subject is heterozygous for the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule.
- 5 15. The method of any one of claims 12 to 14, wherein the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule comprises a splice-site variant, a stop-gain variant, a start-loss variant, a stop-loss variant, a frameshift variant, a missense variant, an in-frame indel variant, and/or a variant that encodes a truncated FNIP1 variant polypeptide or a truncated FLCN variant polypeptide.
- 10 16. The method of any one of claims 12 to 14, wherein the FNIP1 variant nucleic acid molecule comprises any one or more of the genetic variations in Table 8.
17. The method of any one of claims 12 to 14, wherein the FLCN variant nucleic acid molecule comprises any one or more of the genetic variations in Table 9.
18. A method of treating a subject having muscle disorder or at risk of developing muscle disorder by administering a muscle disorder therapeutic agent, the method comprising:
- 15 determining or having determined whether the subject has a Folliculin Interacting Protein 1 (FNIP1) variant nucleic acid molecule and/or a Folliculin (FLCN) variant nucleic acid molecule, by:
- obtaining or having obtained a biological sample from the subject; and
- 20 performing or having performed a sequence analysis on the biological sample to determine if the subject has a genotype comprising an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule; and
- administering or continuing to administer the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and/or an FNIP1 inhibitor and/or an FLCN inhibitor to a subject that is FNIP1 reference and/or FLCN reference;
- 25 administering or continuing to administer the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and/or an FNIP1 inhibitor and/or an FLCN inhibitor to a subject that is heterozygous for the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule; or
- 30 administering or continuing to administer the muscle disorder therapeutic agent in a standard dosage amount to a subject that is homozygous for the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule;

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wherein the presence of the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule indicates the subject has a decreased risk of developing muscle disorder.

19. The method of claim 18, wherein the muscle disorder comprises sarcopenia, Duchenne
5 Muscular Dystrophy, or Pompe disease.
20. The method of claim 18 or claim 19, wherein the FNIP1 inhibitor comprises an inhibitory nucleic acid molecule that hybridizes to an FNIP1 nucleic acid molecule.
21. The method of claim 20, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule, a small interfering RNA (siRNA), and/or a short hairpin RNA
10 (shRNA).
22. The method of claim 21, wherein the inhibitory nucleic acid molecule comprises an siRNA.
23. The method of claim 21, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule.
- 15 24. The method of any one of claims 18 to 23, wherein the FLCN inhibitor comprises an inhibitory nucleic acid molecule that hybridizes to an FLCN nucleic acid molecule.
25. The method of claim 24, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule, a small interfering RNA (siRNA), and/or a short hairpin RNA (shRNA).
- 20 26. The method of claim 25, wherein the inhibitory nucleic acid molecule comprises an siRNA.
27. The method of claim 25, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule.
28. The method of any one of claims 18 to 27, wherein the subject is heterozygous for the
25 FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, and the subject is administered or continued to be administered the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount and the FNIP1 inhibitor and/or FLCN inhibitor.
29. The method of any one of claims 18 to 27, wherein the subject is FNIP1 reference
30 and/or FLCN reference, and the subject is administered or continued to be administered the muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount and the FNIP1 inhibitor and/or FLCN inhibitor.

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30. The method of any one of claims 18 to 29, wherein the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule comprises a splice-site variant, a stop-gain variant, a start-loss variant, a stop-loss variant, a frameshift variant, a missense variant, an in-frame indel variant, and/or a variant that encodes a truncated FNIP1 variant polypeptide or a truncated FLCN variant polypeptide.
31. The method of any one of claims 18 to 29, wherein the FNIP1 variant nucleic acid molecule comprises any one or more of the genetic variations in Table 8.
32. The method of any one of claims 18 to 29, wherein the FLCN variant nucleic acid molecule comprises any one or more of the genetic variations in Table 9.
33. A method of identifying a subject having an increased risk of developing muscle disorder, the method comprising:
- determining or having determined the presence or absence of a Folliculin Interacting Protein 1 (FNIP1) variant nucleic acid molecule and/or a Folliculin (FLCN) variant nucleic acid molecule in a biological sample obtained from the subject;
- wherein:
- when the subject is FNIP1 reference and/or FLCN reference, then the subject has an increased risk of developing the muscle disorder; and
- when the subject is heterozygous or homozygous for the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule, then the subject has a decreased risk of developing the muscle disorder.
34. The method of claim 33, wherein the muscle disorder comprises sarcopenia, Duchenne Muscular Dystrophy, or Pompe disease.
35. The method of claim 34 or claim 35, wherein the FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule comprises a splice-site variant, a stop-gain variant, a start-loss variant, a stop-loss variant, a frameshift variant, a missense variant, an in-frame indel variant, and/or a variant that encodes a truncated FNIP1 variant polypeptide or a truncated FLCN variant polypeptide.
36. The method of any one of claims 33 to 35, wherein the FNIP1 variant nucleic acid molecule comprises any one or more of the genetic variations in Table 8.
37. The method of any one of claims 33 to 35, wherein the FLCN variant nucleic acid molecule comprises any one or more of the genetic variations in Table 9.

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38. The method of any one of claims 33 to 37, further comprising administering a muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and/or an FNIP1 inhibitor and/or an FLCN inhibitor to a subject that is FNIP1 reference and/or FLCN reference.
- 5 39. The method of claim 38, comprising administering a muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and an FNIP1 inhibitor and/or an FLCN inhibitor to a subject that is FNIP1 reference and/or FLCN reference.
40. The method of any one of claims 33 to 37, further comprising administering a muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage
10 amount, and/or an FNIP1 inhibitor and/or an FLCN inhibitor to a subject that is heterozygous for an FNIP1 variant nucleic acid molecule and/or an FLCN variant nucleic acid molecule.
41. The method of claim 40, comprising administering a muscle disorder therapeutic agent in an amount that is the same as or less than a standard dosage amount, and an FNIP1 inhibitor and/or an FLCN inhibitor to a subject that is heterozygous for an FNIP1 variant nucleic acid
15 molecule and/or an FLCN variant nucleic acid molecule.
42. The method of any one of claims 33 to 41, wherein the FNIP1 inhibitor comprises an inhibitory nucleic acid molecule that hybridizes to an FNIP1 nucleic acid molecule.
43. The method of claim 42, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule, a small interfering RNA (siRNA), and/or a short hairpin RNA
20 (shRNA).
44. The method of claim 43, wherein the inhibitory nucleic acid molecule comprises an siRNA.
45. The method of claim 43, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule.
- 25 46. The method of any one of claims 33 to 45, wherein the FLCN inhibitor comprises an inhibitory nucleic acid molecule that hybridizes to an FLCN nucleic acid molecule.
47. The method of claim 46, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule, a small interfering RNA (siRNA), and/or a short hairpin RNA (shRNA).
- 30 48. The method of claim 47, wherein the inhibitory nucleic acid molecule comprises an siRNA.

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49. The method of claim 47, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule.
50. A muscle disorder therapeutic agent for use in the treatment or prevention of muscle disorder in a subject having an FNIP1 variant nucleic acid molecule and/or an FLCN variant
5 nucleic acid molecule.
51. The muscle disorder therapeutic agent of claim 50, wherein the FNIP1 variant nucleic acid molecule and/or the FLCN variant nucleic acid molecule is a splice-site variant, a stop-gain variant, a start-loss variant, a stop-loss variant, a frameshift variant, a missense variant, an in-frame indel variant, or a variant that encodes a truncated FNIP1 or FLCN variant polypeptide.
- 10 52. The muscle disorder therapeutic agent of claim 50 or claim 51, wherein the FNIP1 variant nucleic acid molecule comprises any one or more of the genetic variations in Table 8.
53. The muscle disorder therapeutic agent of claim 50 or claim 51, wherein the FLCN variant nucleic acid molecule comprises any one or more of the genetic variations in Table 9.
54. A Folliculin Interacting Protein 1 (FNIP1) inhibitor for use in the treatment or
15 prevention of muscle disorder in a subject that is FNIP1 reference or is heterozygous for an FNIP1 variant nucleic acid molecule.
55. The FNIP1 inhibitor of claim 54, wherein the FNIP1 variant nucleic acid molecule is a splice-site variant, a stop-gain variant, a start-loss variant, a stop-loss variant, a frameshift variant, a missense variant, an in-frame indel variant, or a variant that encodes a truncated
20 FNIP1 variant polypeptide.
56. The FNIP1 inhibitor of claim 54 or claim 55, wherein the FNIP1 variant nucleic acid molecule comprises any one or more of the genetic variations in Table 7.
57. The FNIP1 inhibitor of any one of claims 54 to 56, wherein the FNIP1 inhibitor comprises an inhibitory nucleic acid molecule that hybridizes to an FNIP1 nucleic acid molecule.
- 25 58. The FNIP1 inhibitor of claim 57, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule, a small interfering RNA (siRNA), and/or a short hairpin RNA (shRNA).
59. The FNIP1 inhibitor of claim 58, wherein the inhibitory nucleic acid molecule comprises an siRNA.
- 30 60. The FNIP1 inhibitor of claim 58, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule.

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61. A Folliculin (FLCN) inhibitor for use in the treatment or prevention of muscle disorder in a subject that is FLCN reference or is heterozygous for an FLCN variant nucleic acid molecule.
62. The FLCN inhibitor of claim 61, wherein the FLCN variant nucleic acid molecule is a splice-site variant, a stop-gain variant, a start-loss variant, a stop-loss variant, a frameshift
5 variant, a missense variant, an in-frame indel variant, or a variant that encodes a truncated FLCN variant polypeptide.
63. The FLCN inhibitor of claim 61 or claim 62, wherein the FLCN variant nucleic acid molecule comprises any one or more of the genetic variations in Table 9.
64. The FLCN inhibitor of any one of claims 61 to 63, wherein the FNIP1 inhibitor
10 comprises an inhibitory nucleic acid molecule that hybridizes to an FNIP1 nucleic acid molecule.
65. The FLCN inhibitor of claim 64, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule, a small interfering RNA (siRNA), and/or a short hairpin RNA (shRNA).
66. The FLCN inhibitor of claim 64, wherein the inhibitory nucleic acid molecule comprises
15 an siRNA.
67. The FLCN inhibitor of claim 64, wherein the inhibitory nucleic acid molecule comprises an antisense nucleic acid molecule.