

AAV-Mediated Gene Transfer Restores a Normal Muscle Transcriptome in a Canine Model of X-Linked Myotubular Myopathy

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Multiple clinical trials employing recombinant adeno-associated viral (rAAV) vectors have been initiated for neuromuscular disorders, including Duchenne and limb-girdle muscular dystrophies, spinal muscular atrophy, and recently X-linked myotubular myopathy (XLMTM). Our previous work on a canine model of XLMTM showed that a single rAAV8-cMTM1 systemic infusion corrected structural abnormalities within the muscle and restored contractile function, with affected dogs surviving more than 4 years post injection. This remarkable therapeutic efficacy presents a unique opportunity to identify the downstream molecular drivers of XLMTM pathology and to what extent the whole muscle transcriptome is restored to normal after gene transfer. Herein, RNA-sequencing was used to examine the transcriptomes of the *Biceps femoris* and *Vastus lateralis* in a previously described canine cohort that showed dose-dependent clinical improvements after rAAV8-cMTM1 gene transfer. Our analysis confirmed several dysregulated genes previously observed in XLMTM mice but also identified transcripts linked to XLMTM pathology. We demonstrated XLMTM transcriptome remodeling and dose-dependent normalization of gene expression after gene transfer and created metrics to pinpoint potential biomarkers of disease progression and correction.

INTRODUCTION

The last 30 years have seen the field of neuromuscular disease (NMD) genetics grow from one known gene for Duchenne muscular dystrophy (DMD) in 1987 to hundreds of disease genes identified today. NMDs are complex diseases whose pathological processes are often not entirely understood. Gene therapy offers a unique treatment approach for single-gene NMDs, because fixing the root cause of the defect does not necessarily require a comprehensive understanding of the pathophysiology. However, successful gene therapy provides an extraordinary opportunity to delve more deeply into the complex molecular underpinnings of disease initiation, progression, and correction.

In the past several years, treatment breakthroughs have been made in small and large animal models of NMDs,^{1–7} while clinical benefits have been reported after a single injection of recombinant adeno-associated virus (rAAV) in patients with spinal muscular atrophy.⁸ In most of these studies, results consisted of correlations between transgene expression levels and clinical outcome measures. However, this level of insight may prove insufficient when sub-therapeutic effects are the outcome or, conversely, when adverse events occur *in vivo*,^{9–11} a limitation that strongly argues for a deeper understanding of disease mechanisms. Therefore, the identification of disease-associated gene dysregulation and signaling pathways that are not—or only partially—corrected after gene transfer is of considerable interest. Also, as more gene therapies are approved for NMDs, it will become increasingly important to track their long-term durability using non-invasive biomarkers that appear prior to clinical deterioration.

Recent advances in -omics technologies have provided valuable tools for the diagnosis of NMDs and for the understanding of disease mechanisms at the molecular level.^{12–16} In this study, we investigated the underlying mechanisms of rAAV-mediated correction of muscle pathology utilizing the canine model of X-linked myotubular myopathy (XLMTM). XLMTM is a centronuclear myopathy caused by mutations in the *MTM1* gene, which encodes the myotubularin protein.¹⁷ Patients exhibit severe muscle weakness, breathing difficulties,

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and a high mortality rate in the first years of life.^{18,19} XLMTM muscle cells have smaller diameters, an abnormal architecture, and poor excitation-contraction coupling (ECC).^{20–23} At the molecular level, myotubularin is involved in phospholipid metabolism, and its absence leads to structural and functional defects in key membrane compartments such as the sarcoplasmic reticulum, the T-tubule network, and the neuromuscular junction.^{20,24–27} In addition, the insulin-like growth factor 1 (IGF1) and downstream signaling pathways (Akt, mTOR, autophagy, ubiquitin-proteasome) are dysregulated, which correlates with marked muscle hypotrophy.^{28–31} During the past decade, the use of rAAV vectors in XLMTM mice and dogs demonstrated remarkable therapeutic efficacy, paving the way for a recently initiated clinical trial,^{3,5,24,32} (ClinicalTrials.gov: NCT03199469). Treated XLMTM dogs showed dose-dependent correction of multiple disease phenotypes, resulting in improved muscle function and survival up to 4 years of age.^{5,33} Here, we explored the transcriptional changes driving this correction of muscle morphology and function in treated XLMTM dogs using an unbiased, comprehensive RNA-sequencing (RNA-seq) approach. Untreated XLMTM dogs exhibited transcriptional changes consistent with well-described disease phenotypes, and several genes emerged as potential candidates to explain disease development and progression. Importantly, rAAV gene therapy leads to a dose-dependent restoration of the muscle transcriptome toward a more normal profile. We also present an array of metrics based on RNA-seq data to quantify gene therapy efficacy and distinguish the transcripts corrected to normal after treatment from those escaping correction. Finally, we highlight potential RNA biomarkers to monitor and predict the efficacy of current and future gene therapy protocols.

RESULTS

Unsupervised Analysis Discriminates XLMTM Dogs According to Treatment Groups

Muscle samples for the RNA-seq analysis herein were obtained from a previous study⁵ in which XLMTM dogs were randomized to receive one of three increasing doses of rAAV8-*cMTM1* or saline as a negative control. Groups were named AAVLow (0.3E+14 vector genomes [vg]/kg), AAVMid (2.0E+14 vg/kg), AAVHigh (5.0E+14 vg/kg), and XLMTM, respectively, and were compared to wild-type (WT) controls (Figure 1A). The AAVMid and AAVHigh doses were characterized as therapeutic with full correction of disease phenotypes such as survival, neurological scores, and muscular and respiratory functions (Figure 1B).⁵ Conversely, the AAVLow dose resulted in sub-therapeutic clinical outcomes, including significant weakness, significant muscle pathology, and death of two animals. In this *a posteriori* study, the transcriptome of these dogs was analyzed using RNA-seq on two muscles of the hindlimb: *Biceps femoris* and *Vastus lateralis*. Due to premature death encountered in the XLMTM and AAVLow groups, dogs were not age matched, but samples were all collected at necropsy to reflect the final extent of disease progression or correction (Table S1). In each muscle, the top 500 most informative genes were selected based on their expression variance across samples and were used for principal component analysis (PCA). It showed segregation of the 13 dogs in 2 groups (Figures 1C and 1D): AAVLow and XLMTM dogs in

one group; WT and AAVHigh dogs in the other. The AAVMid group also clustered with WT and AAVHigh dogs in the *Vastus* and was spread between the two groups in the *Biceps*. Gene ontology analysis was performed on the top 500 genes in each muscle and identified multiple terms related to muscle biology, particularly in the *Vastus* (Figure S1).

rAAV Gene Therapy Remodels the XLMTM Transcriptome in a Dose-Dependent Manner

To gain further insight into the development of XLMTM disease phenotypes in these two muscles, and their correction by gene therapy, we determined the differentially expressed (DE) genes between XLMTM dogs and WT controls using the edgeR package.³⁴ In the *Biceps* and the *Vastus*, 824 and 1,122 DE genes were obtained, respectively. Among them, 400 were identified in both muscles, suggesting overlap in XLMTM disease processes between different muscles. Gene ontology analysis of the 400 common DE genes pointed to muscle development, muscle contraction, and various metabolic responses (Figure 2A). Of note, individual gene deregulations previously identified in XLMTM mice or in human patients were confirmed in the dog model. For instance, three acetylcholine receptor subunits were overexpressed in both muscles of XLMTM dogs: *CHRNA1*, *CHRND*, and *CHRNA3*^{26,35,36} (Figure S2). Ryanodine receptor 1 (*RYR1*) and dihydropyridine receptor (*CACNA1S*) transcript levels were also both upregulated in XLMTM patient cells *in vitro*,³⁷ and this result was confirmed in our datasets, although not significantly. Finally, the growth differentiation factor 8 (myostatin, *MSTN*) and its antagonist follistatin (*FST*) were also respectively down- and upregulated, similar to what was recently observed in *Mtm1*-knockout (KO) mice^{36,38} (Figure S2). Together, these data suggest an overlap between the transcriptome dysregulation induced by XLMTM in different species. The lists of DE genes in both *Biceps* and *Vastus* are available in Tables S2 and S3. Importantly, the expression profiles of the three *CHRN* genes, *MSTN*, and *FST*, were verified by qPCR, and comparison between the different groups of dogs showed a trend almost identical to the RNA-seq data (Figure S3). To visualize the extent of XLMTM transcriptome remodeling achieved by the three injected rAAV doses, we plotted the entire set of DE transcripts from both muscles of XLMTM untreated dogs and all three treatment groups relative to WT control dogs (log fold-change values, log FC) (Figures 2B and 2C). This plot showed that both upregulated and downregulated DE genes (in green and blue, respectively) were corrected, with log FC values progressively returning to zero. The log FC interquartile (IQ) range was then calculated to quantify transcriptome remodeling. This number represents the length of the interval comprising the central half (25%–75%) of ranked log FC values. Therefore, it estimates how the expression values of the DE gene set diverge from WT controls. In the *Biceps*, log FC IQ range values varied from 3.0 to 2.8, 1.3, and 0.91 in untreated XLMTM, AAVLow, AAVMid, and AAVHigh dogs, respectively (Figure 2B). In the *Vastus*, AAVMid dogs had a lower IQ range than AAVHigh dogs, reflecting a higher transcriptome remodeling effect with the intermediate rAAV dose (XLMTM, 2.7; AAVLow, 2.1; AAVMid, 0.81; and AAVHigh, 1.3; Figure 2C). Hierarchical clustering using the common

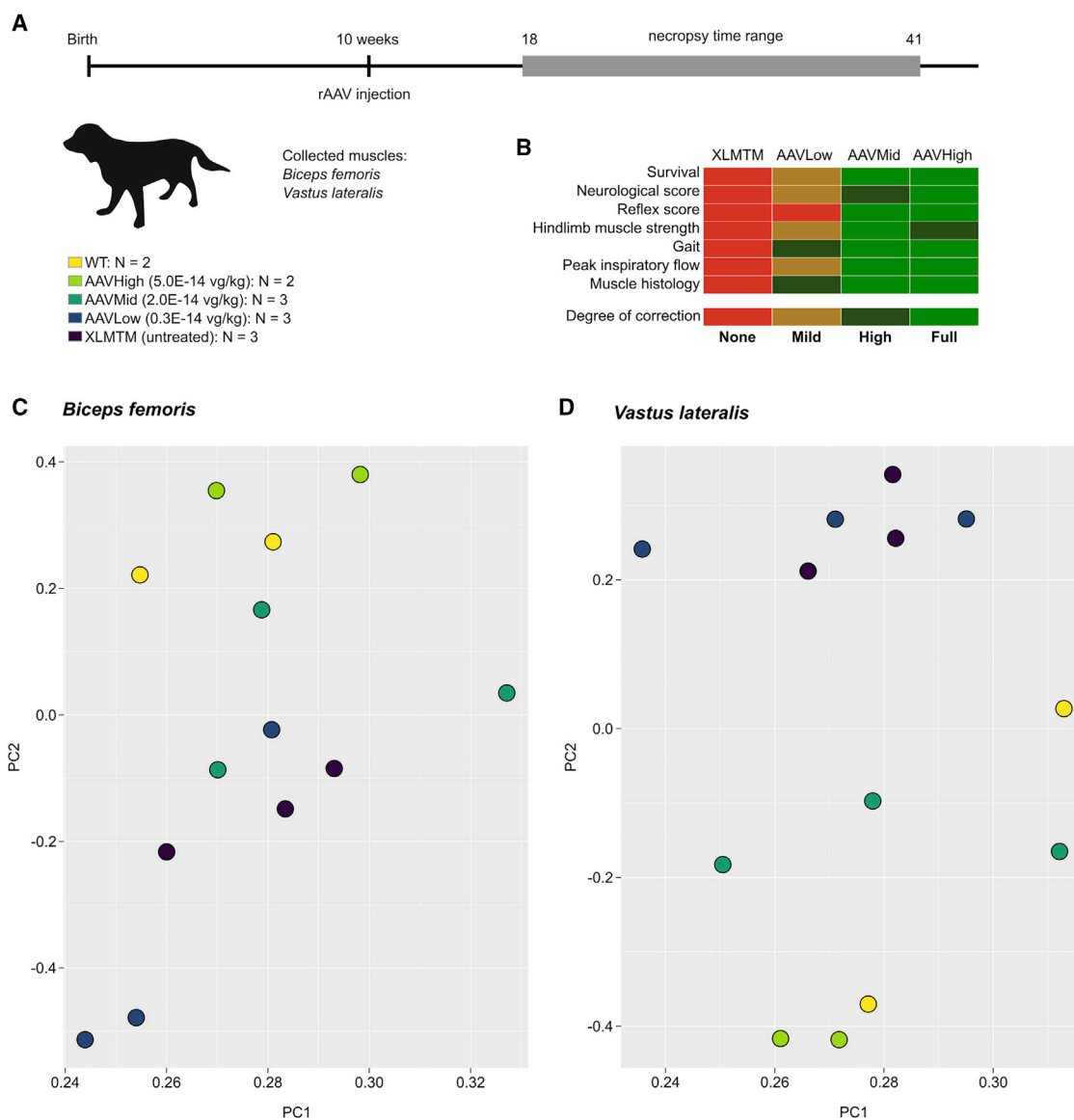
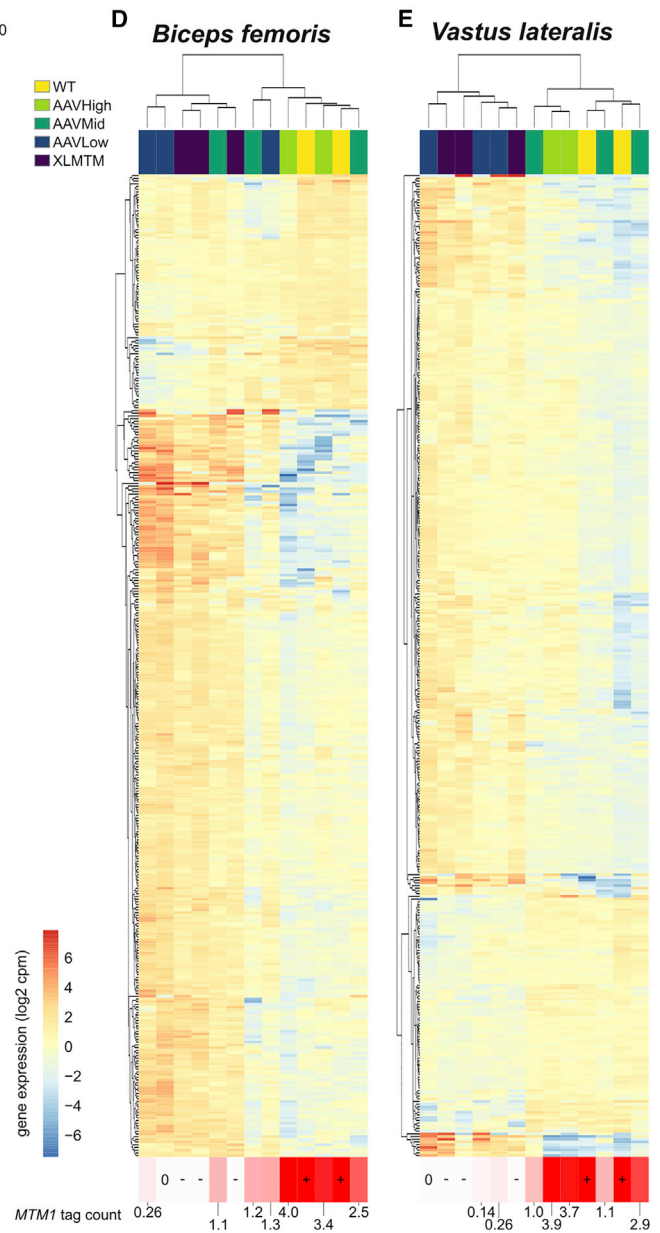
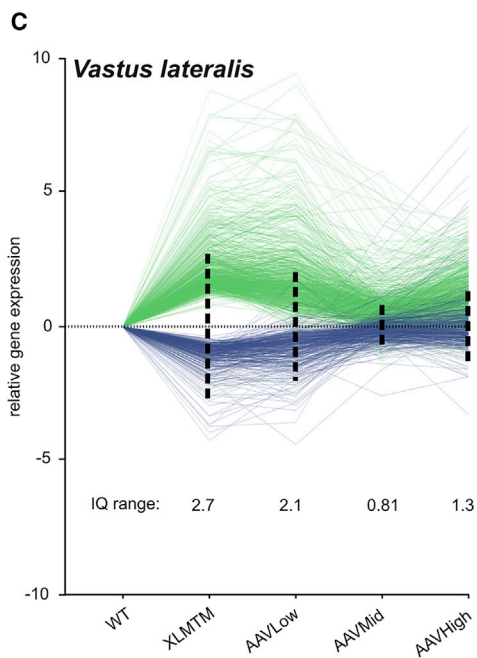
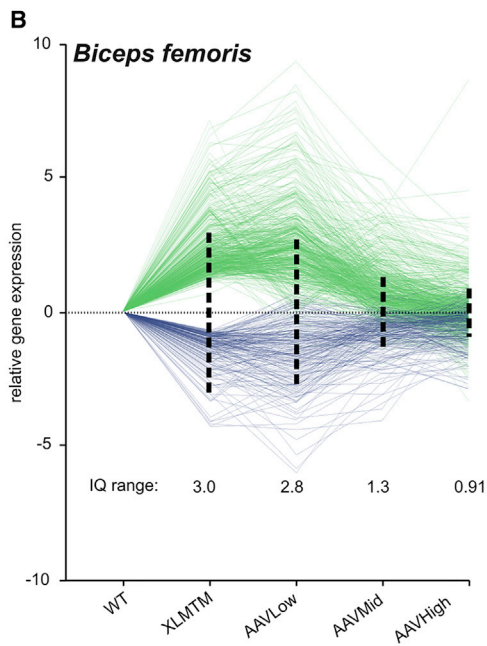
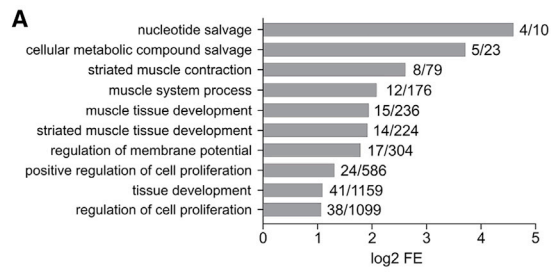


Figure 1. Visualization of Gene Therapy Efficacy by Transcriptome Profiling in XLMTM Dogs

(A) Experimental timeline in weeks and details of the 5 groups of dogs. The rAAV vector was injected at 10 weeks of age, and dogs were monitored until the age of 39 to 41 weeks, unless euthanasia criteria were reached prematurely, as encountered in untreated XLMTM and AAVLow dogs. Additional details are provided in Table 1. (B) Heatmap representing the degree of corrections of key XLMTM phenotypes achieved in the three groups of dogs, as measured in our previous study.⁵ (C) Principal component analysis (PCA) on RNA-seq data in the *Biceps femoris* after selection of the top 500 most informative genes across samples. (D) PCA on RNA-seq data in the *Vastus lateralis* after selection of the top 500 most informative genes across samples. For (C) and (D), PC1 and PC2 were projected in a two-dimensional plot, with each dog represented as a color-coded dot.

DE genes distinguished therapeutic (AAVMid and AAVHigh) and sub-therapeutic (AAVLow) doses (Figure 2D). The only exception was observed between dog 04 (AAVMid) and dog 13 (AAVLow) *Biceps* samples, which clustered with the sub-therapeutic and therapeutic groups, respectively. Interestingly, disease correction in dog 13 (SSAN_18) was more pronounced than in the two other AAVLow dogs, and it did not reach euthanasia criteria before the end of the study period (Table S1).⁵ *MTM1* transgene expression was then

measured directly from RNA-seq data using a custom-made workflow for rAAV-derived mRNA tag counting and showed that transgene expression strongly correlated with the extent of transcriptome correction (Figure 2D). Transgene expression level in dog 13 *Biceps* was comparable to that of AAVMid dogs (*MTM1* tag count = 1.3 versus a median of 1.2 in AAVMid dogs), suggesting that evaluation of transgene expression directly from RNA-seq data is a better predictor of transcriptome remodeling than the injected dose of gene



(legend on next page)

therapy vector and that it reflects itself on overall treatment outcome. Therefore, injected *Biceps* samples were re-ordered in two distinct groups: the *Therapeutic* group with the two AAVHigh dogs, two AAVMid dogs, and dog 13; and the *Sub-therapeutic* group, with the two remaining AAVLow dogs, and dog 04. In the *Vastus*, all AAVMid and AAVHigh clustered together with WT controls and formed the *Therapeutic* group, while AAVLow dogs formed the *Sub-therapeutic* group.

RNA-Seq Allows the Creation of Molecular Metrics of Gene Therapy Efficiency

Because distinct sub-populations of transcripts may respond differently to gene therapy, an array of metrics was created, based on the type of transcriptome remodeling effect. *Rescued* genes were defined as the XLMTM-associated DE genes that were no longer significantly different from WT controls in rAAV-treated dogs (Figure 3A). Conversely, *Resistant* genes were still differentially expressed between rAAV-treated dogs and WT controls. Two additional sub-populations of *Partially Rescued* and *Worsened* genes were also defined but were both marginally represented irrespective of the vector dose. These metrics were determined for the *Sub-therapeutic* and *Therapeutic* groups of dogs, in the *Biceps* and the *Vastus* muscles (Figures 3B and 3C). As anticipated, a sub-therapeutic effect was associated with only 6.1% and 7.5% of genes with a *Rescued* expression profile in the *Biceps* and *Vastus* muscles, respectively, while *Resistant* genes accounted for 64% and 57%. In sharp contrast, the proportion of *Rescued* genes reached 52.1% and 42.7% in the *Biceps* and *Vastus* of the dogs showing therapeutic benefits (Figures 3B and 3C). This indicates that an increase in *MTM1* transgene expression drives a more profound restoration of the muscle transcriptome, providing for the first time a comprehensive transcriptomic explanation of physiological and histological outcome measures observed previously.⁵

Differential Treatment Outcome Leads to Identification of Disease Biomarkers

Next, populations of *Candidate Biomarkers* of XLMTM correction were defined as the genes presenting a *Rescued* expression profile in the *Therapeutic*, but not in the *Sub-therapeutic* group of dogs (Figures 4A and 4B). This resulted in more than 400 genes in each muscle, 120 of which were detected in both *Biceps* and *Vastus*. As expected, the expression pattern of these 120 genes followed a similar trend, with sustained deregulation in the XLMTM and *Sub-therapeutic* groups, and a marked rescue in the *Therapeutic* group (Figures 4C and

4D). In the latter, IQ range values were only 0.45 and 0.61 in the *Biceps* and the *Vastus*, respectively. Finally, a list of 12 candidate biomarkers was isolated among the genes with the most significant expression changes in the two XLMTM muscles (p value < 0.001 in each muscle; Figure 4E) and their expression level was correlated with *MTM1* tag counts in injected dogs and untreated controls (tag counts = 0, by definition). The most significant correlation was obtained for *APEX2*, an endonuclease involved in base-excision repair and progression through the cell cycle (correlation coefficient $\rho = -0.86$, p value = $2.3E-7$). Interestingly, this list also contained *ALAS2* ($r = -0.83$, p value = $1.3E-6$) and *PIK3R2* ($r = -0.82$, p value = $3.3E-6$), two genes that were recently associated with muscle strength,³⁹ and *NRK* ($r = -0.82$, p value = $3.8E-6$), known to be specifically expressed during myotome formation and early muscle development in mice, but not in the adult.⁴⁰ The expression of these 4 genes in injected dogs was inversely correlated with *MTM1* transgene expression. *Candidate Biomarkers* also included *RINI1*, *EFCAB7*, *ANGPTL2*, *CHRNA1*, *PROCR*, *IGF2*, *ETS2*, and *RIMS3* (Figure 4F). Interestingly, two of these genes are known to be secreted in the serum: *IGF2* and *ANGPTL2*. Their expression was validated on independent biopsies by qPCR, which resulted in typical “biomarker” expression profiles (Figures 4G and 4H). The full lists of *Rescued* genes in both muscles and of *Candidate Biomarkers* are available in Tables S4 and S5.

DISCUSSION

With the recent success of preclinical and clinical trials using rAAV vectors, understanding the exact processes by which disease phenotypes are impacted—and eventually rescued—by gene therapy is of considerable interest for the field of molecular medicine. Here, we take advantage of the unprecedented therapeutic efficacy obtained in XLMTM dogs to investigate the molecular mechanisms of NMD correction, with a focus on pathological muscle transcriptome. Overall, our study demonstrates that corrective rAAV gene therapy induces a dose-dependent transcriptome remodeling, which was highly correlated with RNA-seq-based transgene expression measurements. These measures were comparable with our previous study despite being obtained by different techniques on distinct muscle biopsies⁵ and revealed high levels of recombinant *MTM1* transcript in the dogs presenting with full disease correction.

For logistical and ethical considerations, it was decided to include both hemizygous *MTM1*^{-y} male and homozygous *MTM1*^{-/-}

Figure 2. Remodeling of the XLMTM Transcriptome by rAAV Gene Therapy

(A) Gene ontology analysis on the differentially expressed genes common to XLMTM *Biceps* and *Vastus* muscles. For each represented term, the log₂ fold enrichment (FE) values are graphically represented, together with the x/y ratio, defined as the number of genes participating to this enrichment (x) over the total number of genes affiliated with the corresponding ontology (y). (B) Relative expression of the differentially expressed genes in the *Biceps*, expressed in log fold change (log FC) after normalization with healthy controls. The interquartile ranges were determined from positive log FC values (negative log FC were converted into absolute values) and represented as dashed vertical lines pointing in both directions around the $y = 0$ line. (C) Similar representation for the differentially expressed genes detected in the *Vastus* muscle. (D and E) Hierarchical clustering generated from log cpm values of the 400 common differentially expressed genes for the *Biceps* (D) and the *Vastus* (E). Each column represents one muscle sample, color-coded for treatment group; each row represents one individual gene, color coded for its expression level (log cpm). RNA-seq-based *MTM1* mRNA tag counts are indicated under each column.

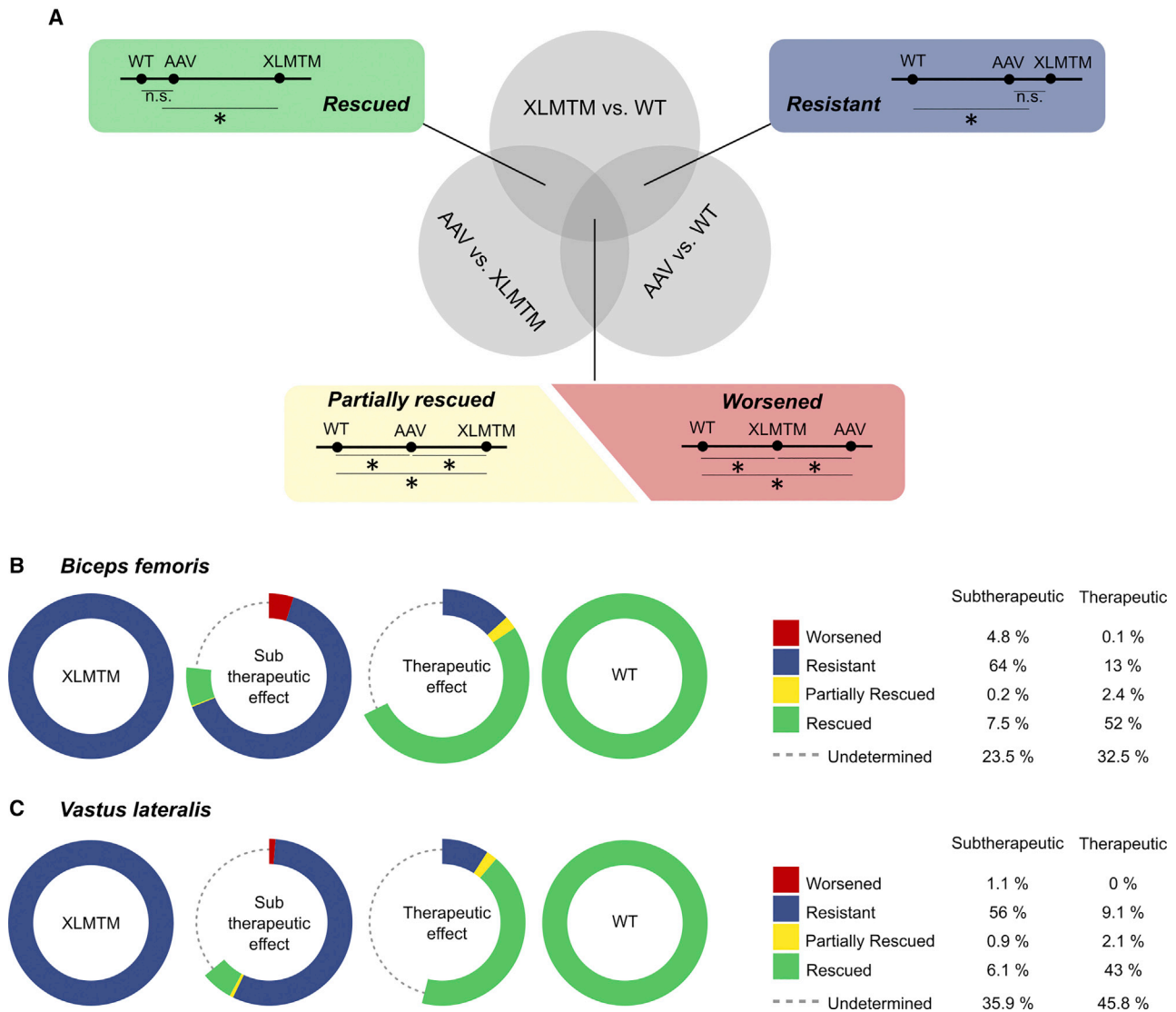


Figure 3. Quantifiers of Transcriptome Remodeling and Gene Therapy Efficacy in XLMTM Dogs

(A) Venn diagram representing the intersections of differentially expressed gene populations obtained after comparison of untreated XLMTM, rAAV-treated XLMTM, and healthy dogs. Focus is made on the *Rescued* and the *Resistant* two-circle domains in specific insets and on the central domain containing *Partially Rescued* and *Worsened* genes. Exemplar gene-expression levels are plotted on a line for the three groups: healthy, XLMTM, and rAAV-treated (AAV) dogs. n.s., non-significant gene expression difference; *, significant difference. (B and C) Evolution of the described metrics in the *Sub-therapeutic* and the *Therapeutic* groups of dogs—as defined in the text—in the *Biceps* (B) and the *Vastus* (C) muscles. The initial DE gene set in XLMTM dogs is represented as a blue ring, and its counterpart in healthy controls as a green ring. In rAAV-treated dogs, the areas corresponding to the above-described metrics have an arc length directly proportional to the proportion of initial DE genes presenting the corresponding expression profile.

female dogs in the study, since they both present comparable XLMTM phenotypes. Dog randomization into the different treatment groups led to uneven distribution of females in the untreated XLMTM and AAVLow groups, and therefore, sex-related differences cannot be entirely ruled out in this study.⁵ Nonetheless, unsupervised analyses have clearly demonstrated that the overall variability was driven by transgene expression, which can distinguish dogs showing therapeutic versus subtherapeutic responses to rAAV treatment.

To our knowledge, this study is one of the first to report a comprehensive transcriptome profile from myotubularin-deficient muscles, and the first in a large animal model. Previously, individual genes were queried in *Mtm1*-deficient mice as an attempt to explain clinical observations.^{26,29,38} In addition, muscle biopsies from 8 XLMTM patients have been analyzed for the expression of 4,200 genes using microarray and pointed to the upregulation of genes coding for cytoskeletal and extracellular matrix proteins.³⁵ More recently, a publication used RNA-seq in *Mtm1δ4* mice treated or not with tamoxifen,

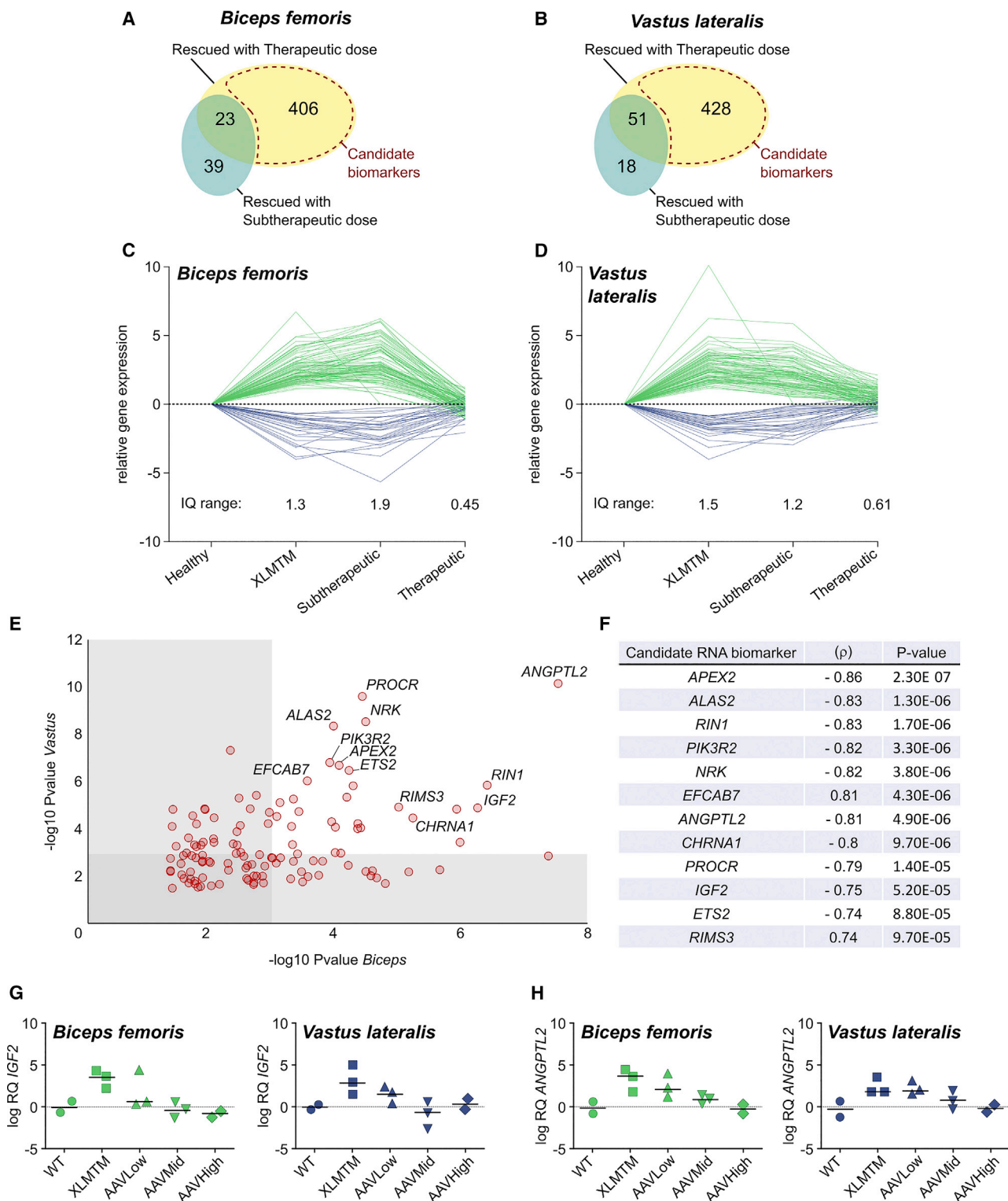


Figure 4. Candidate RNA Biomarkers of AAV Therapeutic Effect in XLMTM Dogs

(A and B) Venn diagrams showing the number of genes with a *Rescued* profile and their overlap between the *Sub-therapeutic* and the *Therapeutic* groups. The *Candidate Biomarker* gene subsets are delineated with a dashed red area, respectively in the *Biceps* (A) and the *Vastus* (B). (C) Relative expression of the candidate biomarkers in the (legend continued on next page)

and highlighted a set of 849 differentially expressed genes between untreated *Mtm1δ4* mice and WT controls.³⁶ In our study, we gathered data on more than 32,000 dog genes, some of them not yet characterized. Importantly, several genes previously identified as differentially expressed in XLMTM patients and mice were also detected in dogs. In comparison with the mouse transcriptome,³⁶ we found an overlap of 87 deregulated ortholog genes in our XLMTM dogs, and ranking of log FC values showed a high correlation between the two species ($\rho = 0.6$, $p = 1.1E-9$) (Table S6).

Among the overlap, we notably found three subunits of the nicotinic acetylcholine receptor: *CHRNA1*, *CHRNA3*, and *CHRNA5*, whose deregulation might be related to the compromised ability of XLMTM muscle cells to generate Ca^{2+} transients in response to electrical stimulation.^{20,21} In this regard, genes coding for *RYR1* and *CACNA1S* are upregulated in XLMTM patients' cells,³⁷ and were also slightly overexpressed in XLMTM dogs, although no significant differences were measured (Figure S2). Interestingly, XLMTM dogs also showed deregulation of multiple additional genes coding for ion transporters that could also lead to ECC defects, including sodium (*SCN4B*, *SCN5A*, *SCNN1A*) and potassium (*KCNK17*, *KCNQ5*) channels, the sodium/potassium-transporting ATPase subunit alpha-3 (*ATP1A3*), and members of the solute carrier (SLC) family.

Another major consequence of myotubularin deficiency is an early muscle hypotrophy observed in patients and animal models.^{22,23,32,41-43} XLMTM myotubes have a small diameter and centrally positioned nuclei, and they are often considered abnormally developed or unable to maintain a fully differentiated state. In XLMTM mice, these characteristics correlate with dysregulated PI3K/Akt/mTOR signaling and abnormal autophagy.^{29,30,44,45} More recently, another study reported the downregulation of the myostatin pathway in *Mtm1*-KO mice, which could be a compensatory mechanism to counter muscle hypotrophy.³⁸ Herein, the genes coding for myostatin (*MSTN*) and follistatin (*FST*) were down- and upregulated, respectively, in XLMTM dogs. These outcomes confirmed the involvement of this pathway downstream of myotubularin deficiency (Figure S2), and the potential of myostatin as a therapeutic target. Indeed, treatment with ActRIIB-mFc, a myostatin inhibitor, resulted in muscle hypertrophy and increased lifespan in XLMTM mice.⁴⁶ More recently, these mice were co-injected with an rAAV vector coding for an inhibitory myostatin propeptide in addition to rAAV-*Mtm1*, and this led to a greater increase in muscle mass than mice treated with rAAV-*Mtm1* only.³⁸ This finding demonstrates that the tools created in our study have the potential to identify relevant targets for combinatorial gene therapy applications.

In light of our RNA-seq data, abnormal muscle development appears as an important component of XLMTM biology in dogs. The genes encoding the myogenic regulators MyoD (*MYOD1*) and myogenin (*MYOG*) are overexpressed in XLMTM dogs, together with *PAX7*, a marker of adult muscle stem (satellite) cells (Tables S2 and S3). In addition, several genes coding for isoforms of structural proteins transiently expressed during skeletal muscle embryonic development were found upregulated, including the acetylcholine receptor γ subunit (*CHRNA3*) and myosin heavy chain 3 (*MYH3*) in the *Biceps*, or cardiac alpha-actin (*ACTC1*) and troponin T (*TNNI3*) in the *Vastus*. Of note, XLMTM dogs reached euthanasia criteria prematurely and their median age at necropsy was 22 weeks, as opposed to 39 weeks in WT dogs. At this age, muscles are expected to be in their terminally differentiated state, as seen by histological examination. However, subtle differences in their transcriptome cannot be ruled out and might confound the expression of developmental genes. Overall, transcriptome profiling of canine XLMTM muscles not only confirmed gene-expression data in mice and human patients, but also helped identify multiple genes not previously associated with XLMTM biology, and whose deregulation provides insight into disease phenotypes.

Gene therapy studies rarely investigate the molecular consequences of target cell transduction. With rAAV vectors injected in new patients every year, now including boys suffering from XLMTM (clinical trial NCT03199469), a better understanding of the molecular mechanisms by which NMDs are corrected will become crucial. Recently, one study reported the normalization of microarray gene expression data after dual rAAV gene therapy in a mouse model of oculopharyngeal muscular dystrophy (OPMD).⁶ Concerning XLMTM, tamoxifen-treated *Mtm1δ4* mice only showed 29 differentially expressed genes compared to untreated controls,³⁶ but these data were obtained at an earlier time after treatment compared to our study. In these two publications,^{6,36} the authors did not focus on specific genes or gene sub-populations. Herein, we provide for the first time a comprehensive picture of muscle transcriptome remodeling after rAAV gene therapy using RNA-seq. We used hierarchical clustering to group injected dogs based on the extent of transcriptome remodeling rather than on the dose of rAAV injected *in vivo*. In agreement with previous clinical observations,⁵ this clustering approach resulted in a *Sub-therapeutic* and a *Therapeutic* group of dogs. Strikingly, the *Biceps* sample collected from dog 13 was part of the *Therapeutic* group despite a treatment with an otherwise sub-therapeutic dose of vector. However, inclusion in the *Therapeutic* group correlated with the extended lifespan and phenotypic improvements observed in this specific dog.⁵ To illustrate different facets of transcriptome remodeling, we created several metrics and

Biceps (C) and the *Vastus* (D), expressed in log FC after normalization with healthy controls. The interquartile ranges were determined from positive log FC values (negative log FC were converted into absolute values). (E) Two-dimensional dot-plot of the 120 candidate biomarkers common to the *Biceps* and *Vastus* muscles, representing the significance of the differential expression between XLMTM dogs and healthy controls (p values). Each dot represents one gene. (F) Selection of twelve RNA biomarkers of gene therapy efficacy in XLMTM dogs, ranked according to their correlation coefficient (ρ) when compared to *MTM1* mRNA tag counts. The significance of this correlation is indicated (p -value). (G and H) *IGF2* (G) and *ANGPTL2* (H) expression levels in both muscles assessed by qRT-PCR normalized with the housekeeping gene *RPL32* and represented relative to WT dogs; RQ, relative quantity = $2^{-\Delta\Delta Ct}$; log, base 2 logarithm.

determined the proportion of genes whose expression was normalized or not after treatment (Figure 3A). We demonstrated that these metrics can be used to identify dogs exhibiting therapeutic benefits from those in which gene therapy efficacy was not durable. In specific cases, it may also be used to determine transcripts that have been induced by gene therapy treatment as a side effect independent of phenotypic correction. More precisely, this population corresponds to genes that are deregulated in treated dogs but not in their untreated counterparts, when compared to WT controls. Herein, we detected only marginal proportions of genes presenting this expression pattern, which correlates with the absence of adverse events, and of any humoral or cellular immune responses against the transgene product in rAAV-injected dogs.⁵ Overall, we obtained confirmation that treatment was well-tolerated at the level of the muscle transcriptome.

Finally, this analytical approach proved very effective to identify RNA biomarkers of XLMTM correction. Interestingly, several of the top 12 candidate genes not only align with XLMTM phenotypes but could also help deepen our understanding of disease development: *ALAS2* and *PIK3R2* have recently been negatively associated with muscle strength in a meta-analysis of more than 7,500 human subjects³⁹ and were also found overexpressed in XLMTM dogs; Nik-related kinase (NRK) is a protein kinase involved in actin polymerization through phosphorylation and inhibition of cofilin, is only expressed during embryonic myogenesis,⁴⁰ and is overexpressed in XLMTM dogs, which adds to the list of dysregulated developmental genes; *APEX2* encodes an endonuclease physically associated with proliferating cell nuclear antigen (PCNA) and driving cell-cycle progression through base-excision repair on the replicative nuclear and mitochondrial DNA.^{47,48} *APEX2* is also overexpressed in untreated XLMTM muscles and corrected in the *Therapeutic* group, suggesting that de-regulation/re-regulation of the cell cycle is a key component of disease development and rescue. Altogether our data provide a transcriptional characterization of the structural immaturity encountered in XLMTM muscles.

RNA biomarkers defined in this study could also help identify protein products known to be secreted in the blood and, therefore, would be easily quantifiable. In this regard, at least two genes highlighted in our list could be further investigated at the protein level: angiopoietin-like protein 2 (*ANGPTL2*), an inflammatory mediator participating in blood vessel formation, and insulin-like growth factor 2 (*IGF2*). Recently, increased *ANGPTL2* expression has been reported in a mouse model of denervation-induced muscle atrophy, and when knocked out, improved muscle growth and satellite cell activity.⁴⁹ Herein, *ANGPTL2* is overexpressed in untreated XLMTM dogs, and reduced to basal levels in the *Therapeutic* group. Thus, *ANGPTL2* itself might be an important mediator of rAAV-mediated therapeutic benefits. As a proinflammatory cytokine, it is accurately quantifiable in blood samples, and is already used in the context of colorectal cancer.⁵⁰ This makes it an excellent candidate biomarker to monitor the evolution of XLMTM after clinical gene therapy.

In conclusion, this study brings evidence of XLMTM rescue by rAAV gene therapy at the molecular level, in the form of a dose-dependent transcriptome remodeling acting on specific aspects of disease biology. Furthermore, it introduces an array of RNA biomarkers in the form of individual genes or carefully defined gene populations, which brings unprecedented insight to the mechanisms of NMD rescue by gene therapy.

MATERIALS AND METHODS

Animal Model

The XLMTM Labrador/Beagles used in this study have a p.N155K mutation in the *MTM1* gene and were issued from a colony maintained at the University of Washington.^{3,41} More precisely, they were previously included in a gene therapy study, the methods and results of which were extensively described in a recent publication.⁵ Animal experimentation was reviewed and supervised by the University of Washington Institutional Review Board. In brief, XLMTM dogs were infused with three increasing doses of a rAAV vector expressing a canine *MTM1* cDNA: 0.3E+14, 2.0E+14, and 5.0E+14 vg/kg at the age of 10 weeks, and sacrificed between 39 and 41 weeks old or when reaching humane euthanasia criteria. In the absence of treatment, XLMTM dogs, both hemizygous males and homozygous females, exhibit progressive clinical deterioration between about 12 and 26 weeks of age, resulting in an inability to stand, walk, and feed. Eight injected dogs were included in this study, together with 3 untreated XLMTM and 2 WT controls, as summarized in Table S1. Necropsy samples were collected from two muscles of the hindlimb to increase statistical power and not restrict the analysis to only one replicate per dog.

RNA Extraction and Sequencing

Muscle necropsy tissues were frozen on dry ice and stored at $\leq -60^{\circ}\text{C}$. RNA extraction, library preparation, and sequencing on an Illumina HiSeq 4000 were conducted by Genewiz (NJ, USA). Specifically, total RNA was extracted with QIAGEN AllPrep mini kit. RNA samples were quantified using a Qubit 2.0 Fluorometer (Life Technologies, Carlsbad, CA, USA) and RNA integrity was checked with an RNA Screen Tape on an Agilent 2200 TapeStation (Agilent Technologies, Palo Alto, CA, USA). RNA sequencing library preparation was prepared with a TruSeq Stranded mRNA Library Prep kit following the manufacturer's protocol (Illumina, category number RS-122-2101). Sequencing libraries were validated using a DNA Analysis Screen Tape on the Agilent 2200 TapeStation (Agilent Technologies, Palo Alto, CA, USA), and quantified by using the Qubit 2.0 Fluorometer (Invitrogen, Carlsbad, CA), as well as by qPCR (Applied Biosystems, Carlsbad, CA, USA). Sequencing libraries were multiplexed and clustered on flow cell using the cBOT from Illumina. After clustering, the flow cell was loaded on the Illumina HiSeq instrument according to manufacturer's instructions. The samples were sequenced using a 2×150 Pair-End (PE) High Output configuration. Image analysis and base calling were conducted by the HiSeq Control Software (HCS) on the HiSeq instrument. Raw sequence data (.bcl files) generated from Illumina HiSeq was converted into fastq files and de-multiplexed using Illumina bcl2fastq program version 2.17. One mismatch was allowed for index sequence identification. The 13

Table 1. Details of the Primers, Probe, and Gene-Expression Arrays Used in the qRT-PCR Validation Experiment

	Forward primer	5'-TGGTTACGGGAGCAACAAGAAA-3'
	Reverse primer	5'-GCACATCAGCAGCACTTCA-3'
<i>RPL32</i>	Probe	5'-TGCTGCCCACTGGCTTCTGG-3' - VIC-QSY
<i>CHRNA1</i>	Thermo Fisher Scientific – TaqMan Gene Expression - Cf02621957_m1 - FAM/MGB-NFQ	
<i>CHRND</i>	Thermo Fisher Scientific – TaqMan Gene Expression - Cf02691404_m1 - FAM/MGB-NFQ	
<i>CHRNA1</i>	Thermo Fisher Scientific – TaqMan Gene Expression - Cf02704147_m1 - FAM/MGB-NFQ	
<i>IGF2</i>	Thermo Fisher Scientific – TaqMan Gene Expression - Cf02693069_m1 - FAM/MGB-NFQ	
<i>FST</i>	Thermo Fisher Scientific – TaqMan Gene Expression - Cf02645950_m1 - FAM/MGB-NFQ	
<i>MSTN</i>	Thermo Fisher Scientific – TaqMan Gene Expression - Cf02704228_m1 - FAM/MGB-NFQ	
<i>ANGPTL2</i>	QIAGEN - qRT-PCR ² primer assay for dog ANGPTL2 – product 330001	

Vastus-mRNA-derived libraries were sequenced to an average of 60 M paired-end reads/sample and the 13 *Biceps*-mRNA-derived libraries were sequenced to an average of 20 M paired-end reads/sample.

RNA Extraction and qRT-PCR

Dog tissues were homogenized using MagNa Pure LC RNA Isolation Tissue Lysis Buffer (Roche) and total RNA was isolated using automated nucleic acid extraction instruments, MagNA Pure 96 System (Cellular RNA Large Volume Kit [Roche]; 350 μ L sample input, 50 μ L sample output). RNA was subject to DNase treatment to remove genomic DNA contamination (Ambion, DNA-free DNA Removal Kit, Life Technologies) and reverse transcribed using random hexamers and RevertAid H minus Reverse Transcriptase (Fermentas) (250 ng of total RNA). qPCR was performed in a LightCycler 480 system (Roche) by using 4 μ L of 1/10 diluted cDNA, SyberGreen mix (Thermo Fisher Scientific) (*ANGPTL2*), Taqman Gene Expression (Thermo Fisher Scientific) (*CHRNA1*, *CHRND*, *CHRNA1*, *IGF2*, *FST*, *MSTN*) and primers (*RPL32*) listed below (Table 1).

Data Analysis

Initial data analysis, including alignment to reference genome and count table generation, was conducted on the DNAnexus platform (Palo Alto, CA, USA). Specifically, fastq files were first mapped onto the reference genome of *Canis lupus familiaris* (genome assembly: CanFam3.1 [GCA_000002285.2], downloaded from <https://www.ensembl.org>) using the Subread mapping package^{51,52} (settings: subread-align -t 0 -T 4 -d 50 -D 600 -i my_index -r read1 -S ff -R read2 -o \$output_name). The resulting bam files were fed into featureCounts⁵¹ package to obtain the count-per-gene table (settings: featureCounts -p -P -d 50 -D 600 -t exon -g gene_id -a GTF_file -o \$output_name bam_file1 bam_file2 bam_file3 bam_file4 bam_file5

bam_file6 bam_file7 bam_file8 bam_file9 bam_file10 bam_file11 bam_file12 bam_file13). Count tables were further analyzed with the open-source RStudio environment for R (<https://www.r-project.org/>) and the Bioconductor software (<https://www.bioconductor.org/>). The limma⁵² and edgeR³⁴ packages were used to normalize, fit, and compare the data between groups following the analysis pipeline detailed here.⁵³ Cutoff values for DE gene determination were as follows: p value < 0.05 and fold-change (FC) > 2.0. The code used to analyze count tables is comprehensively detailed in the [Supplemental Information](#). Gene ontology analyses were performed on the GO consortium online platform (<http://geneontology.org/>), using the statistical overrepresentation test and the Bonferroni correction for multiple testing. Enrichments with a corrected p value lower than 0.05 were considered significant.

Data Representation

Heatmaps and PCA plots were automatically generated in R-Bioconductor. Other data representations were realized on Graphpad PRISM 7 and figures were assembled using the vector graphics Inkscape software. The color palette used in this manuscript to distinguish dog groups was extracted from the viridis package on R-Bioconductor and was carefully selected to be easily interpretable by individuals with colorblindness (<https://cran.r-project.org/web/packages/viridis/vignettes/intro-to-viridis.html>).

Data Availability

The RNA-sequencing data from this publication have been deposited to the Sequence Read Archive (SRA) database (<https://www.ncbi.nlm.nih.gov/sra>), and assigned the Bioproject ID PRJNA49575. The read files are available at the following link: <https://trace.ncbi.nlm.nih.gov/Traces/sra/sra.cgi?study=SRP165150>.

SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at <https://doi.org/10.1016/j.ymthe.2019.10.018>.

AUTHOR CONTRIBUTIONS

J.-B.D. designed and performed the experiments, analyzed the data and wrote the manuscript. J.G. designed the experiments, analyzed the data, and assisted in drafting the manuscript. E.R.-G., K.P., and V.L. performed the experiments and analyzed the data. M.W.L. processed the canine muscle samples and assisted in drafting the manuscript. R.W.G. performed the assessments of muscle force and assisted in drafting the manuscript. J.T.G. designed the experiments and assisted in drafting the manuscript. A.B.-B. provided the gene therapy vector, designed the experiments, and assisted in drafting the manuscript. M.K.C. designed the experiments. D.L.M. designed the experiments, analyzed the data, and wrote the manuscript.

CONFLICTS OF INTEREST

M.W.L. is a member of advisory boards for Audentes Therapeutics, Solid Biosciences, and Ichorion Therapeutics. He is also a consultant for Wave Life Sciences and Dynacure. A.B.-B. and M.K.C. are inventors of a patent on gene therapy for myotubular myopathy.

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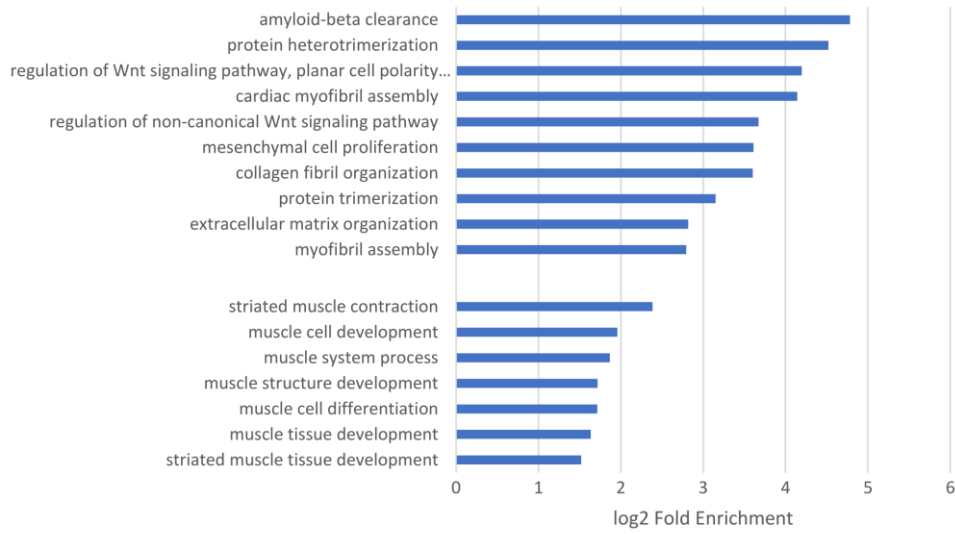
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Supplemental Information

**AAV-Mediated Gene Transfer Restores a Normal
Muscle Transcriptome in a Canine Model
of X-Linked Myotubular Myopathy**

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Gene Ontology TOP 500 *Biceps*



Gene Ontology TOP 500 *Vastus*

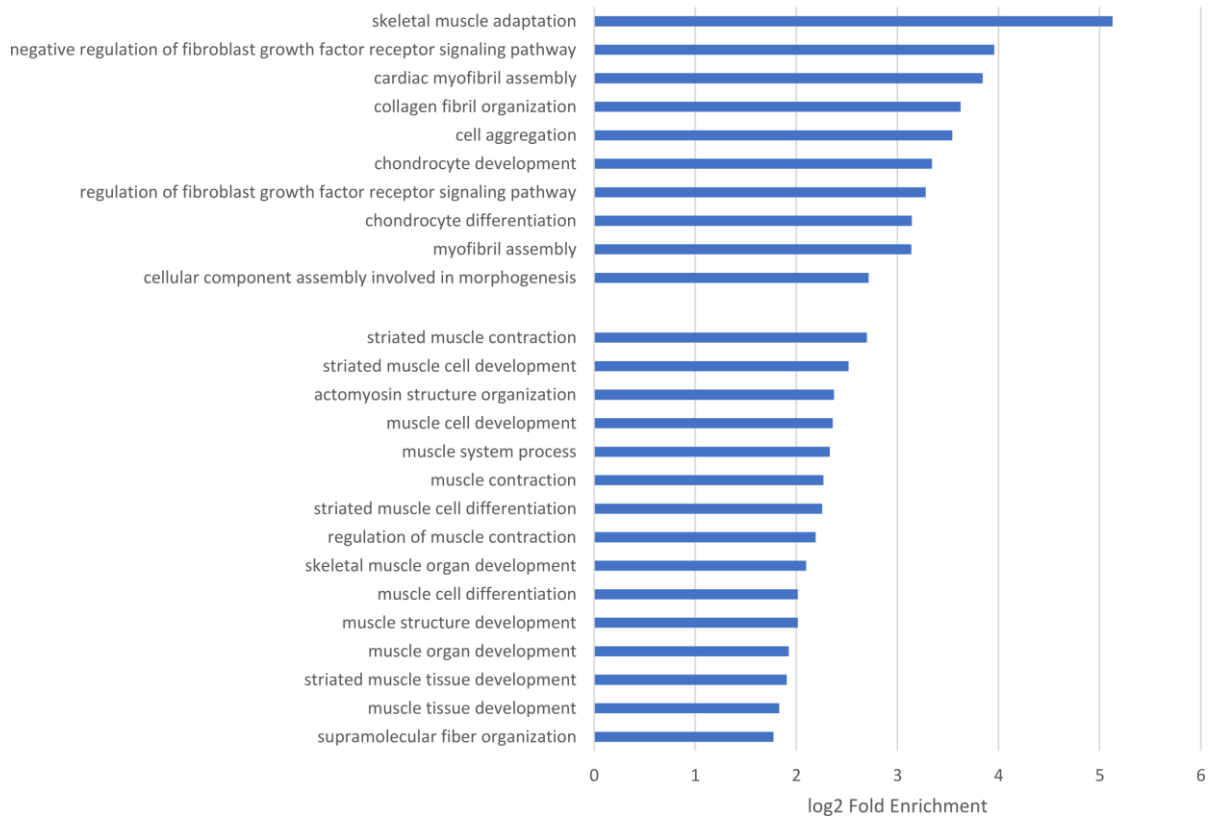
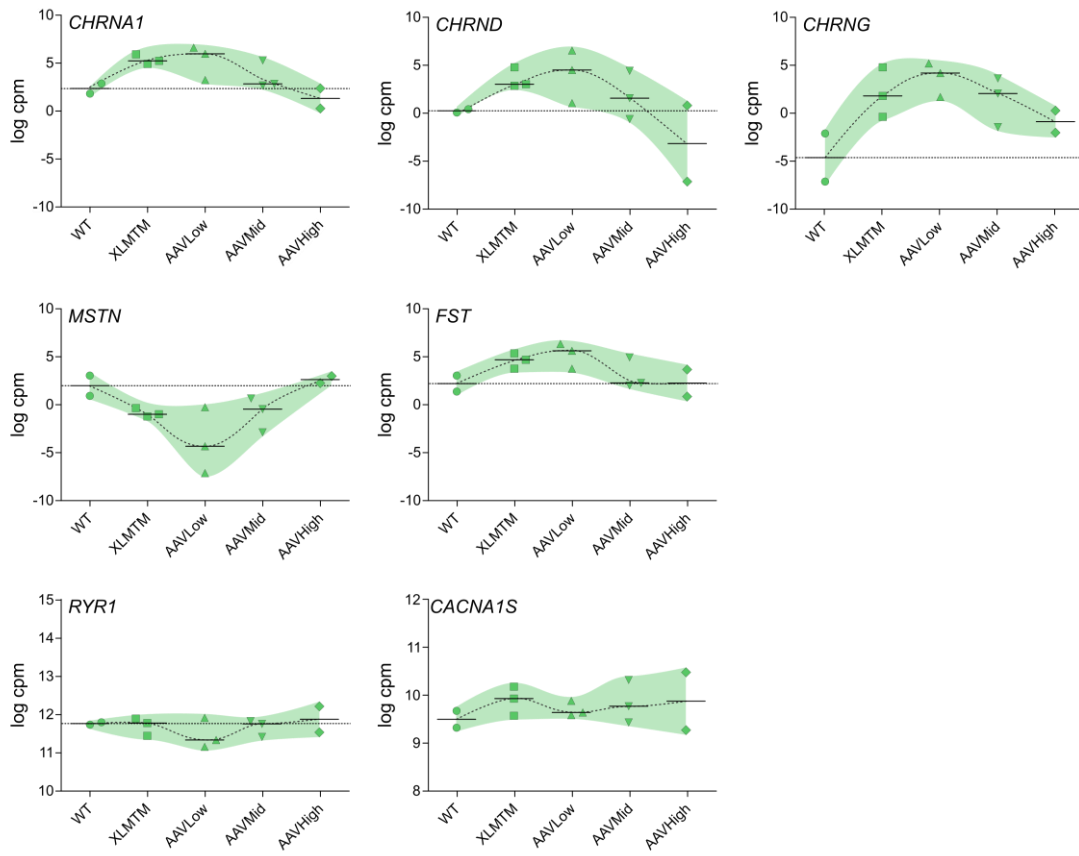


Figure S1: Gene ontology analysis of the TOP 500 most informative genes.

Gene ontology analysis of the 500 genes with the highest expression variance across samples in the *Biceps femoris* (top) and *Vastus lateralis* (bottom). The 10 GO terms with the highest fold enrichment (FE) are represented, and the muscle-related terms with a log₂ FE > 1.

A Biceps femoris



B Vastus lateralis

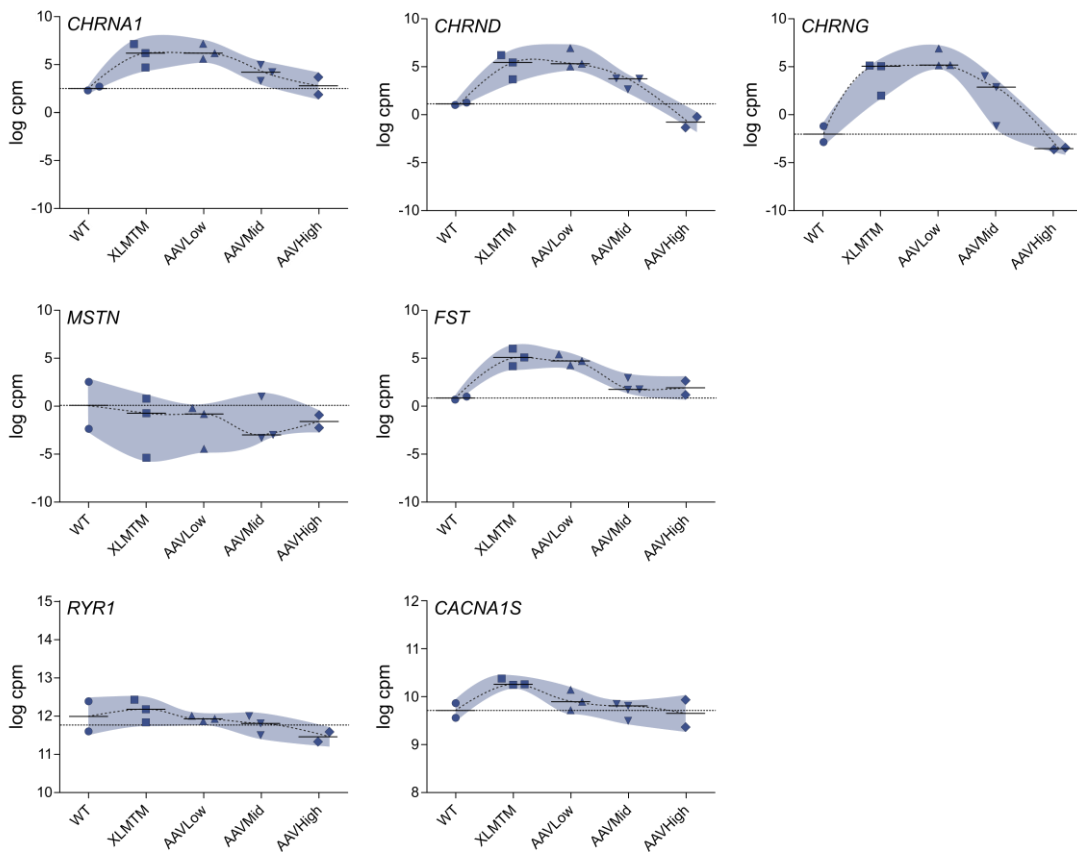
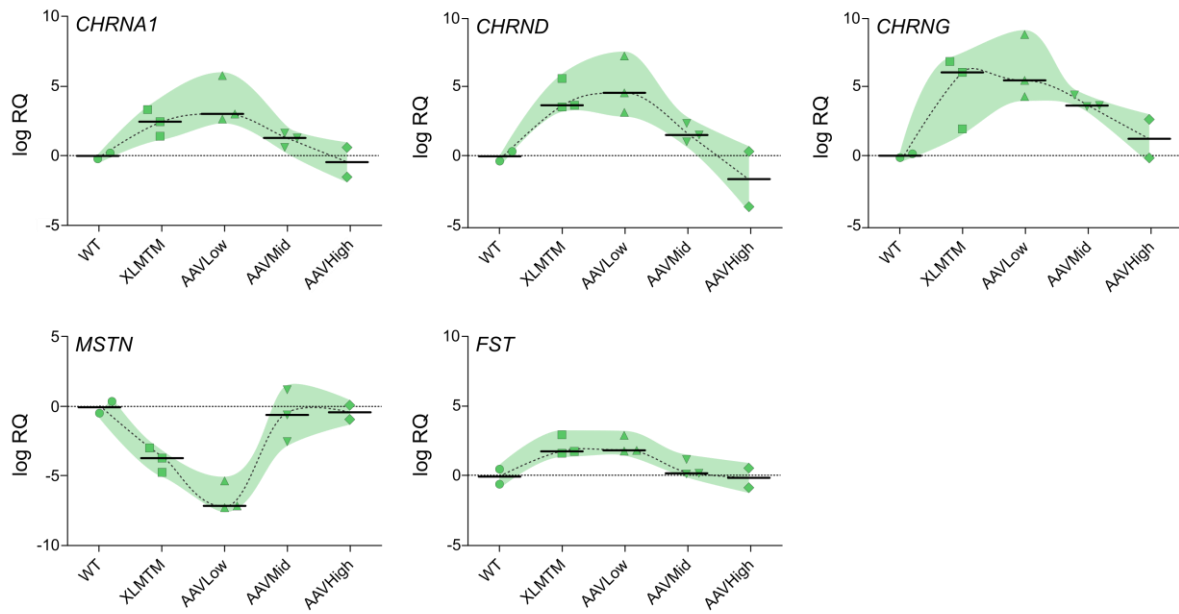


Figure S2: Expression of individual genes associated with XLMTM in mice and human patients from RNA-Seq data in dogs.

Gene expression data (log cpm) for three genes encoding cholinergic receptor subunits (*CHRNA1*, *CHRNA2*, *CHRND*), two myokines: myostatin (*MSTN*) and follistatin (*FST*), and two genes involved in excitation-contraction coupling: ryanodine receptor 1 (*RYR1*) and dihydropyridine receptor (*CACNA1S*) in the *Biceps femoris* (**A**) and the *Vastus lateralis* (**B**). Each symbol represents one individual dog. The median expression in healthy controls is shown as a horizontal dashed line, the expression range as a shaded area, and the evolution of the median as a dashed curve. cpm: count per million reads, log: base 2 logarithm.

A *Biceps femoris*



B *Vastus lateralis*

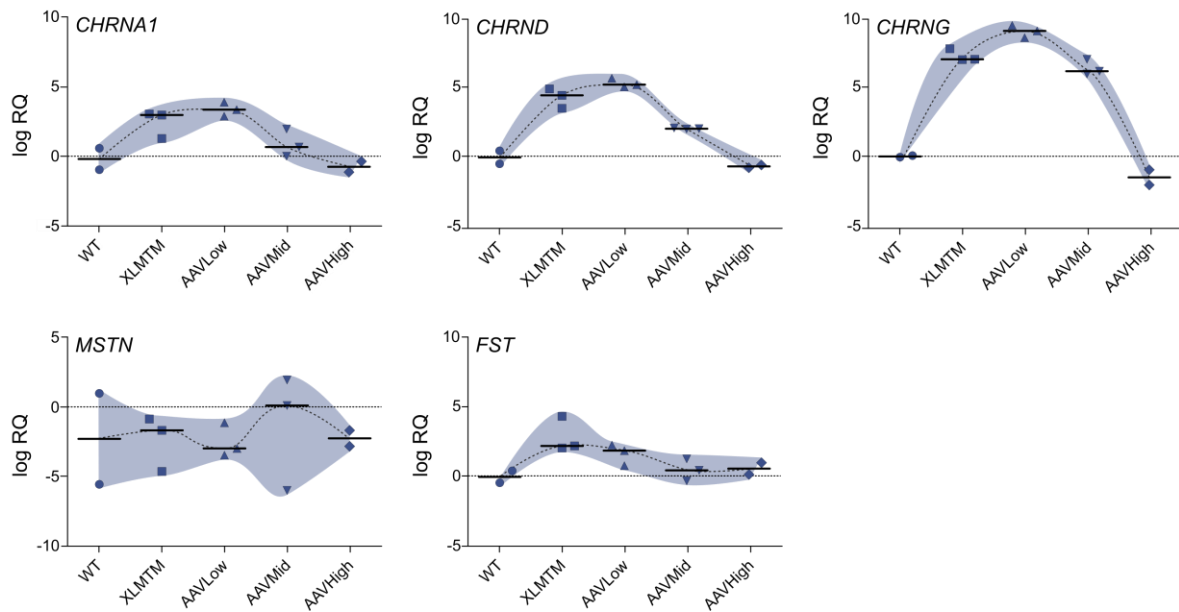


Figure S3: Expression of individual genes associated with XLMTM from RT-qPCR data in dogs.

Gene expression data (log RQ) for *CHRNA1*, *CHRNG*, *CHRND*, *MSTN* and *FST* in the *Biceps femoris* (A) and the *Vastus lateralis* (B). Each symbol represents one individual dog. The median expression in healthy controls is shown as a horizontal dashed line, the expression range as a shaded area, and the evolution of the median as a dashed curve. RQ: relative quantity after normalisation with the median value in the WT group, and the housekeeping gene *RPL32*. log: base 2 logarithm.

SSAN ID	Dog #	Dog ID	Group	Genotype	Gender	Treatment	Necropsy
SSAN_2	Dog 03	HEALTHY1	healthy	WT	Male	Untreated	39 weeks
SSAN_12	Dog 09	HEALTHY2	healthy	WT	Male	Untreated	39 weeks
SSAN_9	Dog 06	XLMTM1	XLMTM	XLMTM	Female	Untreated	18 weeks
SSAN_13	Dog 10	XLMTM2	XLMTM	XLMTM	Female	Untreated	22 weeks
SSAN_16	Dog 12	XLMTM3	XLMTM	XLMTM	Male	Untreated	26 weeks
SSAN_8	Dog 05	AAVLOW1	AAVLow	XLMTM	Male	Low dose	24 weeks
SSAN_11	Dog 08	AAVLOW2	AAVLow	XLMTM	Female	Low dose	28 weeks
SSAN_18	Dog 13	AAVLOW3	AAVLow	XLMTM	Male	Low dose	39 weeks
SSAN_4	Dog 04	AAVMID1	AAVMid	XLMTM	Male	Mid dose	39 weeks
SSAN_10	Dog 07	AAVMID2	AAVMid	XLMTM	Male	Mid dose	41 weeks
SSAN_14	Dog 11	AAVMID3	AAVMid	XLMTM	Male	Mid dose	39 weeks
SSAN_104	Dog 14	AAVHIGH1	AAVHigh	XLMTM	Male	High dose	39 weeks
SSAN_132	Dog 16	AAVHIGH2	AAVHigh	XLMTM	Male	High dose	39 weeks

SSAN ID	Dose (vg/kg)	vg/dg <i>Biceps</i>	vg/dg <i>Vastus</i>	<i>MTM1</i> expression <i>Biceps</i>	<i>MTM1</i> expression <i>Vastus</i>	<i>MTM1</i> mRNA tag counts <i>Biceps</i>	<i>MTM1</i> mRNA tag counts <i>Vastus</i>
SSAN_2	NA	NA	NA	NA	NA	NA	NA
SSAN_12	NA	NA	NA	NA	NA	NA	NA
SSAN_9	NA	NA	NA	NA	NA	0,00E+00	0,00E+00
SSAN_13	NA	NA	NA	NA	NA	0,00E+00	0,00E+00
SSAN_16	NA	NA	NA	NA	NA	0,00E+00	0,00E+00
SSAN_8	3,00E+13	0,23	0,058	4,80E-03	4,00E-03	2,00E-01	0,00E+00
SSAN_11	3,00E+13	0,15	0,24	2,70E-04	4,60E-04	0,00E+00	2,00E-01
SSAN_18	3,00E+13	0,19	0,17	1,70E-04	4,70E-04	1,40E+00	1,00E-01
SSAN_4	2,00E+14	0,82	0,63	1,90E-03	6,90E-03	1,20E+00	1,00E+00
SSAN_10	2,00E+14	1,5	1,1	3,10E-03	5,70E-03	4,80E+00	6,50E+00
SSAN_14	2,00E+14	1,9	0,77	1,00E-02	6,50E-03	1,30E+00	1,20E+00
SSAN_104	5,00E+14	3,6	2,5	6,10E-02	3,30E-02	9,60E+00	1,38E+01
SSAN_132	5,00E+14	2,1	2,7	2,70E-02	8,50E-02	1,53E+01	1,16E+01

Table S1: Details of the dog colony included in this study. Injected rAAV doses are expressed as vector genomes per kilogram (vg/kg); Biodistribution values (vector genomes per diploid genomes, or vg/dg) and *MTM1* expression were determined in a previous publication; *MTM1* tag counts were computed from RNA-seq data.

Table S2: List of differentially expressed genes in the Biceps femoris muscle of untreated XLMTM dogs, compared to WT controls; logFC: base 2 logarithm of the expression fold change (XLMTM / WT).

ensembl ID	Gene name	logFC	PValue
ENSCAFG0000000097	ERBB3	1.9985494	0.0332438
ENSCAFG0000000110	MYL6B	1.8797503	0.0002234
ENSCAFG0000000124	TIMELESS	1.6642717	0.0006016
ENSCAFG0000000225		2.1282097	0.0154395
ENSCAFG0000000282	HECA	-1.2301175	1.41E-06
ENSCAFG0000000288		1.2670245	0.0202622
ENSCAFG0000000372	UST	1.1944214	0.0184217
ENSCAFG0000000413	MTHFD1L	2.3592436	0.0340819
ENSCAFG0000000420	CPM	2.2756181	0.005788
ENSCAFG0000000448	DDR1	1.6574917	1.82E-05
ENSCAFG0000000456	THAP2	-1.1867888	0.0043387
ENSCAFG0000000510	PRR16	5.0845169	0.0003611
ENSCAFG0000000523		1.7383973	3.97E-05
ENSCAFG0000000535	MYCT1	-1.1354123	0.0451202
ENSCAFG0000000561	MIOX	-2.6739231	0.0171164
ENSCAFG0000000577	TIAM2	2.2271125	0.0003346
ENSCAFG0000000611	MEGF10	1.0430251	0.0223794
ENSCAFG0000000617	DDAH2	1.1560715	0.0387498
ENSCAFG0000000670	RIMS2	1.1761648	0.0305624
ENSCAFG0000000722	ADAMTS19	1.7618594	0.0083134
ENSCAFG0000000733		-1.3355278	0.035446
ENSCAFG0000000761	ATF6B	1.0228041	0.001874
ENSCAFG0000000799	ACSL6	-1.2224653	0.0373349
ENSCAFG0000000886	DSE	1.4838567	0.0161702
ENSCAFG0000000903	COL11A2	2.5544118	0.0006814
ENSCAFG0000000934	COL14A1	1.4646104	0.0428096
ENSCAFG0000001007	FBXO32	-1.1817054	0.000267
ENSCAFG0000001049	PMM1	1.0466784	0.0274554
ENSCAFG0000001067	RSPO3	2.1888589	0.0153841
ENSCAFG0000001085	SLC25A48	-1.9601675	0.0453536
ENSCAFG0000001086	MYC	1.3094711	0.0163336
ENSCAFG0000001106	LAMA2	1.4344417	0.0147378
ENSCAFG0000001178	COL22A1	7.4573344	0.0025803
ENSCAFG0000001286	FANCC	-1.03245	0.0181054
ENSCAFG0000001287	TCP11	-1.0920636	0.004375
ENSCAFG0000001290	AKR1B1	-1.0269683	0.0389057
ENSCAFG0000001346	RPL3	1.0253515	0.0048694
ENSCAFG0000001402	KDEL3	1.4323736	0.00394
ENSCAFG0000001426	COPG2	1.045375	0.0014912
ENSCAFG0000001450	MEST	1.1179495	0.0186534
ENSCAFG0000001531	SMO	1.3277523	0.0002888
ENSCAFG0000001533	TSPAN33	1.5150165	0.003072
ENSCAFG0000001537	FREM1	1.503814	0.0008517
ENSCAFG0000001550	FOXRED2	1.2566791	0.0018539
ENSCAFG0000001556	KCNK17	1.911231	0.003774

ENSCAFG00000001581	ADAMTSL1	-1.380429	0.0497587
ENSCAFG00000001596	FOXP4	1.4087347	0.002101
ENSCAFG00000001646	PRUNE2	3.9494118	0.000148
ENSCAFG00000001649	GCNT1	1.8660306	0.0252955
ENSCAFG00000001715	MOB3B	-1.0691933	0.0040969
ENSCAFG00000001718	LRRC4	1.5438732	0.0279787
ENSCAFG00000001793	BTBD11	1.5986254	0.0004039
ENSCAFG00000001875	CKAP4	1.3618483	0.0004823
ENSCAFG00000001909	KIF24	1.5888741	0.0191826
ENSCAFG00000001921		1.0944313	0.0017021
ENSCAFG00000001923	DNAI1	2.369146	0.0223892
ENSCAFG00000001967	C11H9orf131	1.3019602	0.0068244
ENSCAFG00000001985		1.1720133	0.047631
ENSCAFG00000002029	SLC25A27	1.7397346	0.0015148
ENSCAFG00000002046	GNG11	-1.0073856	0.0397899
ENSCAFG00000002069	COL1A2	1.7595663	0.0230639
ENSCAFG00000002079	KDR	-1.5741134	0.0044802
ENSCAFG00000002124	ASB4	-1.0883557	0.026295
ENSCAFG00000002313	OGN	1.5683242	0.0495788
ENSCAFG00000002319	KIAA1211L	1.907257	0.0098455
ENSCAFG00000002397	SHB	1.1487295	0.0376851
ENSCAFG00000002463	THADA	1.0425448	0.0489215
ENSCAFG00000002517		1.0618587	0.0029055
ENSCAFG00000002549	CCDC30	1.702937	0.014782
ENSCAFG00000002645	KCNQ5	1.3076355	0.0204323
ENSCAFG00000002656	EEF1A1	1.1526119	0.0002931
ENSCAFG00000002719		-1.1616372	0.0014733
ENSCAFG00000002748		1.3142511	5.48E-05
ENSCAFG00000002793	IRAK1BP1	1.4637036	0.0446567
ENSCAFG00000002796	CCDC88A	1.2007863	0.0016092
ENSCAFG00000002830	RIMS3	-3.9995339	1.15E-05
ENSCAFG00000002854	IGLON5	3.2561771	0.0016178
ENSCAFG00000002917	AEBP1	2.9819573	0.0001523
ENSCAFG00000002927	CCDC85A	-1.2465901	0.0389786
ENSCAFG00000002928	SVEP1	1.6089033	0.0291748
ENSCAFG00000002940	FANCL	1.2110468	0.0186004
ENSCAFG00000003008	C11H9orf84	2.6678407	0.0180982
ENSCAFG00000003068	NT5C1A	-1.1484772	0.0148455
ENSCAFG00000003096	PM20D2	2.336963	0.0042426
ENSCAFG00000003276	ANTXR1	1.0594788	0.0208935
ENSCAFG00000003290	THAP5	-1.1654024	6.96E-06
ENSCAFG00000003327	COL27A1	1.4750289	0.0345493
ENSCAFG00000003340	AKNA	1.3638802	0.0168268
ENSCAFG00000003388	SH3D21	1.2546736	0.0042817
ENSCAFG00000003415	ODC1	1.3276303	0.0011529
ENSCAFG00000003426	TNC	2.2162376	0.0274508
ENSCAFG00000003458	MMS22L	1.4704712	0.0238038
ENSCAFG00000003528	TCAF1	1.2339108	6.77E-05
ENSCAFG00000003530		1.2723109	0.0088103
ENSCAFG00000003602	DLGAP3	-3.0273129	0.0152416

ENSCAFG00000003663	GSN	1.0990708	0.0203371
ENSCAFG00000003676		-1.1229354	0.0104563
ENSCAFG00000003680	MYLK3	4.1453483	0.0077244
ENSCAFG00000003720	NRCAM	3.5965642	0.0004244
ENSCAFG00000003775	OSR1	3.0713999	0.0013638
ENSCAFG00000003804		3.7122274	0.0011818
ENSCAFG00000003810	PPIL6	1.6225708	0.0234597
ENSCAFG00000003816	SMPD2	1.7334732	9.75E-05
ENSCAFG00000003824	MICAL1	1.6120148	0.0015947
ENSCAFG00000003941	SPATA6	1.5506013	0.0137541
ENSCAFG00000003952	PRKAR2B	-1.3138355	0.0003656
ENSCAFG00000003960	TRAF3IP2	1.3352398	0.0305248
ENSCAFG00000003991	ARHGAP42	1.2132886	0.0088559
ENSCAFG00000004034	EMP3	1.3421992	0.0049694
ENSCAFG00000004094	DLL1	1.2356588	0.0139221
ENSCAFG00000004127	SESN3	2.238837	0.0005788
ENSCAFG00000004128	BBS7	1.0808872	0.0010358
ENSCAFG00000004129	ENDOD1	1.2077503	0.0425102
ENSCAFG00000004176	PANX1	1.9866858	0.0030761
ENSCAFG00000004279	MYO3A	2.4560244	0.0122156
ENSCAFG00000004297	CCDC8	3.5793053	4.82E-08
ENSCAFG00000004331		1.2700819	0.039599
ENSCAFG00000004392	DMPK	1.6211355	3.22E-07
ENSCAFG00000004481	SLC6A6	1.4696773	0.0151837
ENSCAFG00000004492	GRIP2	1.4909129	0.0018855
ENSCAFG00000004510	CDC42EP4	1.2054268	0.0072079
ENSCAFG00000004521	FGD5	-1.0615834	0.0247926
ENSCAFG00000004529	VIM	1.0635385	0.0097079
ENSCAFG00000004555	RARRES2	1.3785828	0.013323
ENSCAFG00000004589		1.4814383	4.41E-06
ENSCAFG00000004636	BCAM	1.2950915	0.0030819
ENSCAFG00000004731	TENM4	1.2159264	0.0150583
ENSCAFG00000004746	XRCC1	1.4936749	0.0004644
ENSCAFG00000004757	PHLDB3	1.4590743	0.0124691
ENSCAFG00000004767	CAD	1.0603273	0.025034
ENSCAFG00000004769	OPTN	-1.3753578	2.56E-05
ENSCAFG00000004785	IFT122	1.0453382	0.0337815
ENSCAFG00000004816	LLGL2	-1.3801129	1.34E-06
ENSCAFG00000004820	ITGA9	1.7450106	0.0118668
ENSCAFG00000004856	PROSER2	2.837645	0.0039736
ENSCAFG00000004866	USP6NL	1.2535465	0.0258327
ENSCAFG00000004916	H3F3B	1.0246086	0.0015366
ENSCAFG00000004931	PLCD1	1.3246758	0.0255963
ENSCAFG00000004958	ATP1A3	-2.1202771	0.0023034
ENSCAFG00000005002	TIMP4	-1.6479683	0.014841
ENSCAFG00000005081	INSIG1	-1.2274206	0.0005203
ENSCAFG00000005122	ST6GALNAC2	-1.0318111	0.0336524
ENSCAFG00000005179	CAPN5	1.1688158	0.0269347
ENSCAFG00000005276	AKR1C3	-1.7824195	0.0250211
ENSCAFG00000005286	SPTBN4	1.6113971	0.0325019

ENSCAFG00000005294	TK1	1.7790676	1.88E-05
ENSCAFG00000005301	PSD3	1.9034447	0.0103111
ENSCAFG00000005309	LBH	1.4633129	0.0288686
ENSCAFG00000005338	BLVRB	1.1160045	0.0155426
ENSCAFG00000005348	EHD3	1.9949194	0.0109675
ENSCAFG00000005411	OSBPL10	1.3275133	0.033281
ENSCAFG00000005433	ABCC4	-1.0520078	0.0234388
ENSCAFG00000005468	PFKP	1.1144971	0.0240206
ENSCAFG00000005490	KCNE3	-1.4390698	0.0313692
ENSCAFG00000005505	PGM2L1	-2.0765818	0.0021838
ENSCAFG00000005527	P4HA3	1.6524674	0.0438637
ENSCAFG00000005530	ZFP36	1.2676883	0.0338014
ENSCAFG00000005564	UCP2	1.7294193	4.62E-05
ENSCAFG00000005595	FARP1	-1.9240399	0.0026851
ENSCAFG00000005621	BHLHE40	-1.6394166	1.37E-05
ENSCAFG00000005671	LRRC3B	-2.2832445	0.0417716
ENSCAFG00000005768	FOLR2	1.4761881	0.0005574
ENSCAFG00000005843	LTBP1	1.3917725	0.001155
ENSCAFG00000005870	RASGRP3	-1.1556743	0.020389
ENSCAFG00000005906	PYCR1	1.0372012	0.0499938
ENSCAFG00000005918	ITGBL1	1.9319822	0.0222555
ENSCAFG00000005965	FOXO1	2.0143814	0.0089946
ENSCAFG00000006006	FASN	1.2944023	0.001018
ENSCAFG00000006019	FREM2	1.8096944	0.0042032
ENSCAFG00000006053		2.2460045	1.22E-06
ENSCAFG00000006065	PRNP	1.0685898	0.0233865
ENSCAFG00000006073	POSTN	2.2391343	0.0285317
ENSCAFG00000006089	SMOX	1.1999842	0.0313584
ENSCAFG00000006091	KITLG	-1.3918214	0.0439853
ENSCAFG00000006106	PCDHB4	1.9949895	0.0492364
ENSCAFG00000006134	KERA	1.9144364	0.0086623
ENSCAFG00000006162	SMAD9	2.0206298	7.25E-05
ENSCAFG00000006164	CYP1B1	2.4875799	0.0150899
ENSCAFG00000006175	CDC25B	1.4340212	0.0437163
ENSCAFG00000006231	DCLK1	3.8517736	8.65E-05
ENSCAFG00000006234	ADAM33	1.4705508	0.0291379
ENSCAFG00000006240	MCF2L	-1.1343084	0.0090496
ENSCAFG00000006255	NBEA	1.0127911	0.0099608
ENSCAFG00000006373		1.252037	0.0065335
ENSCAFG00000006381	SEMA3C	1.5015106	2.65E-05
ENSCAFG00000006424	GXYLT2	1.9611447	0.0018458
ENSCAFG00000006474	PGGHG	1.5468268	0.0176196
ENSCAFG00000006513		-1.1631644	0.0337534
ENSCAFG00000006560	NCAPH	-1.6782798	0.0101947
ENSCAFG00000006576	WDFY4	1.8083009	0.0084989
ENSCAFG00000006582	TMEM80	1.1967136	0.0103567
ENSCAFG00000006596	ANKS1B	2.2046688	0.0028154
ENSCAFG00000006607	DPYSL3	1.5482832	0.0003571
ENSCAFG00000006660	SLC7A1	-1.1137345	0.0004671
ENSCAFG00000006703	UHRF1BP1L	1.2006648	0.0254162

ENSCAFG0000006723	SYT9	1.305997	0.0136821
ENSCAFG0000006788	MTIF3	1.2252995	0.0400223
ENSCAFG0000006797		1.1522907	0.003321
ENSCAFG0000006800	FZD10	2.6678761	3.24E-06
ENSCAFG0000006801	HSPB6	1.0177213	0.011063
ENSCAFG0000006865	PAMR1	2.8225838	0.0366888
ENSCAFG0000006877	FAM110A	2.131169	0.0026386
ENSCAFG0000006909	LMO1	-1.0000269	0.0476376
ENSCAFG0000007001		-1.1892256	0.0047148
ENSCAFG0000007047	MAL	1.6662122	0.0043244
ENSCAFG0000007079		1.327442	0.000195
ENSCAFG0000007111	LGI4	1.7969568	0.0119873
ENSCAFG0000007136	TNFRSF19	1.3172106	0.0169519
ENSCAFG0000007149	FBLN7	2.7991707	0.0020696
ENSCAFG0000007246	CYP7B1	1.734161	0.0040176
ENSCAFG0000007247	ANKRD1	2.6989036	0.0114543
ENSCAFG0000007295	SREK1IP1	-1.1670811	0.0037901
ENSCAFG0000007338	NR4A1	-1.6583959	0.0339885
ENSCAFG0000007344	MYBL1	2.3065726	0.0003029
ENSCAFG0000007358	KCTD15	1.0389654	0.0289894
ENSCAFG0000007465	RHPN2	-1.1797517	0.0149815
ENSCAFG0000007486	CEP89	1.3602764	0.0023939
ENSCAFG0000007562	AMPD3	2.6718334	0.0020755
ENSCAFG0000007635	CLSTN2	2.1583657	0.0069246
ENSCAFG0000007750	CASP3	1.0988799	0.0003011
ENSCAFG0000007770	LNPEP	1.095146	0.0093588
ENSCAFG0000007847	TIMM10	-1.319757	2.77E-05
ENSCAFG0000007853	SAP30	-1.0310148	0.0051343
ENSCAFG0000007893	RBP4	1.9676277	0.0006577
ENSCAFG0000007936	ASB14	-1.3153049	0.0122949
ENSCAFG0000007945	PROCR	2.1209574	4.34E-05
ENSCAFG0000007985	PLCE1	-1.2551266	0.0185598
ENSCAFG0000008026		3.0904792	0.0023537
ENSCAFG0000008062		-2.6542478	0.0033238
ENSCAFG0000008123	TENM3	1.0424926	0.036091
ENSCAFG0000008164	TMEM154	1.9035179	0.0346694
ENSCAFG0000008168	TIGD4	2.2436324	0.0183034
ENSCAFG0000008178	GDAP1	-1.0982379	0.0337935
ENSCAFG0000008236		1.4913865	0.0064784
ENSCAFG0000008288	GPD1	-1.0214588	0.0321299
ENSCAFG0000008295	BTG3	1.8138395	8.55E-05
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ENSCAFG0000008319	CHODL	2.0231766	0.0014243
ENSCAFG0000008333	TMEM161B	-1.0084087	0.0001793
ENSCAFG0000008353	SFRP2	3.748625	0.0208011
ENSCAFG0000008418	NCAM2	1.7019764	0.0121552
ENSCAFG0000008477	BLNK	-1.181329	0.0180735
ENSCAFG0000008519	RTKN	1.3820235	0.0070425
ENSCAFG0000008582	VCAN	1.6419977	0.0260995
ENSCAFG0000008597	ANGPT2	-1.8793916	0.0019207

ENSCAFG00000008640	TUBA1B	1.419475	0.0022979
ENSCAFG00000008661		1.3778535	0.0013452
ENSCAFG00000008707	CKMT2	-1.2174245	0.0028461
ENSCAFG00000008755	SRC	1.5829432	0.0194801
ENSCAFG00000008786	NNAT	1.8604092	0.0003864
ENSCAFG00000008795	FKBP11	1.0520454	0.0209391
ENSCAFG00000008830	TRAFD1	1.0914067	0.0091799
ENSCAFG00000008847	KRTAP11-1	6.1451797	0.0022926
ENSCAFG00000008860	PAQR3	-1.2955411	0.0305646
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ENSCAFG00000008942	C18H11orf49	2.1313221	0.0014805
ENSCAFG00000008975	THBS4	1.6809482	0.0054384
ENSCAFG00000008977	LRP4	1.6413104	0.0054414
ENSCAFG00000008978	EVA1C	2.3088181	0.0058465
ENSCAFG00000009005	CYP26B1	4.7051139	4.05E-05
ENSCAFG00000009017	PPP1R16B	-1.6980186	0.0096029
ENSCAFG00000009022	TMEM64	1.2981223	0.014941
ENSCAFG00000009061	SLC8B1	1.0017663	0.0408296
ENSCAFG00000009066	MYOD1	1.2792955	0.0177768
ENSCAFG00000009076	PLBD2	1.7185704	0.0087959
ENSCAFG00000009096	LXN	1.0015599	0.0260509
ENSCAFG00000009097	SDSL	2.9901595	0.0026625
ENSCAFG00000009104	STC1	1.5147805	0.0179325
ENSCAFG00000009105	FAM92A	2.0433652	0.0018501
ENSCAFG00000009149	SMIM4	-1.0919755	0.0096576
ENSCAFG00000009187	LOXL2	1.4560932	0.0462805
ENSCAFG00000009214	DCBLD2	1.1738957	0.0011786
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ENSCAFG00000009329	PDLIM2	1.9559681	0.0124188
ENSCAFG00000009333	CES1	-3.4388203	0.0018738
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ENSCAFG00000009363	MAPK8IP1	1.2391063	0.0184794
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ENSCAFG00000009414	CHAC1	7.599053	0.0002984
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ENSCAFG00000009506	ABI3BP	1.5258207	0.0405543
ENSCAFG00000009510	EXD1	1.5941081	0.0003677
ENSCAFG00000009569	SPP1	-4.323991	0.0043623
ENSCAFG00000009596	RUNX1	2.8815053	0.0005218
ENSCAFG00000009632	TYRO3	2.0040869	0.0001808
ENSCAFG00000009638	ABCG2	1.6343402	0.0321226
ENSCAFG00000009649	PLEKHA6	1.5979977	0.033564
ENSCAFG00000009653	DOP1B	1.2841788	0.023787
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ENSCAFG00000009721	ALCAM	1.5618096	0.0057404

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ENSCAFG0000009951	SPAG17	4.4146001	0.0046066
ENSCAFG0000009972	ADAMTS8	3.6585067	0.0298222
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ENSCAFG00000010077	LSP1	1.0056485	0.0163783
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ENSCAFG00000010121	CD81	1.4512175	7.66E-05
ENSCAFG00000010142	SLC39A10	1.0400604	0.0299879
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ENSCAFG00000010175	CDH22	-2.4595502	0.0016223
ENSCAFG00000010186	RAB29	-1.2470001	0.0005853
ENSCAFG00000010225	PHKB	-1.0820698	0.0010003
ENSCAFG00000010239	IKBKE	1.2959729	0.0060096
ENSCAFG00000010274	CHI3L1	5.7851446	6.00E-06
ENSCAFG00000010285	ABCG1	4.4374559	0.0015662
ENSCAFG00000010288	MYBPH	3.5261957	0.0001335
ENSCAFG00000010298	ADORA1	4.1882323	1.99E-07
ENSCAFG00000010309	MYOG	1.845086	0.0002147
ENSCAFG00000010395	ADAMTS16	4.4817655	6.24E-06
ENSCAFG00000010408	MLEC	-1.039298	0.0176709
ENSCAFG00000010423	COL4A4	2.2444751	0.0217273
ENSCAFG00000010432	TIRAP	-1.0758181	0.0350677
ENSCAFG00000010496	YARS2	-1.0233588	0.0025834
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ENSCAFG00000010581	CYB561D2	1.3088232	0.014197
ENSCAFG00000010588	MARCKSL1	2.7707109	0.0023246
ENSCAFG00000010593	GSTO1	1.3344276	0.0104336
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ENSCAFG00000010698	LTO1	-1.0143746	0.0090374
ENSCAFG00000010716	TPCN2	1.1272684	0.043151
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ENSCAFG00000010815	TGFB2	2.2452102	1.75E-06
ENSCAFG00000010823	ZBTB20	1.5619384	0.0043654
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ENSCAFG00000010874	SULF2	-1.5770631	0.0281543
ENSCAFG00000010883	FMO5	-1.3040493	0.0009988
ENSCAFG00000010925	HFE	2.0423876	1.27E-06
ENSCAFG00000010936	NPNT	3.5606977	2.55E-06
ENSCAFG00000010982	FAM20A	1.620957	0.0408181
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ENSCAFG00000011330	NEK7	-1.0911281	2.14E-05
ENSCAFG00000011336	MARC1	-1.5080368	0.0101459
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ENSCAFG00000011426	PTGIS	1.6365529	0.0078697
ENSCAFG00000011428	KRAS	-1.0043451	0.0109602
ENSCAFG00000011458	LRMP	2.4578377	0.0126301
ENSCAFG00000011477	BSN	2.5773378	0.0037533
ENSCAFG00000011498	SGSM1	2.4600022	0.0008814
ENSCAFG00000011542	HAPLN3	1.6162553	0.0423641
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ENSCAFG00000011646	ZFHX2	1.7450498	0.0124095
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ENSCAFG00000011682	XIRP2	1.3134881	0.0092161
ENSCAFG00000011744	LAMB2	1.4917481	6.01E-05
ENSCAFG00000011745	SORL1	1.2493712	0.0385312
ENSCAFG00000011817	COL18A1	1.0466518	0.0480526
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ENSCAFG00000011921	ASB11	-1.0674039	0.0032952
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ENSCAFG00000011964	GCNT7	1.4583412	0.0391818
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ENSCAFG00000012022		1.9845705	0.000157
ENSCAFG00000012039	ZNF710	1.2893167	0.0385898
ENSCAFG00000012046	IFI6	2.2650207	0.0034025
ENSCAFG00000012095	AHDC1	1.1151061	6.09E-05
ENSCAFG00000012152	GABBR1	1.1737669	0.0289307
ENSCAFG00000012175	SLC26A6	-1.6185167	0.0010282
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ENSCAFG00000012376	VASH2	2.1323489	0.0029083
ENSCAFG00000012428	HES6	2.0126644	0.0210662
ENSCAFG00000012432	MYOZ2	1.6092946	0.0394641
ENSCAFG00000012493	PFKFB4	-1.7922405	0.0243999
ENSCAFG00000012525	MUC13	4.2271254	3.81E-05
ENSCAFG00000012556	HTRA1	1.560124	0.0017622
ENSCAFG00000012742	MTFP1	-1.5381091	0.0029954
ENSCAFG00000012803	RIN1	3.4011473	4.51E-07
ENSCAFG00000012805	SLC25A12	-1.1238026	0.017736
ENSCAFG00000012824	SCN4B	-1.5043535	0.0112979
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ENSCAFG00000012860	RAPH1	1.2051238	0.0024533
ENSCAFG00000012904	CDK1	1.86909	0.0303179
ENSCAFG00000012925	PHKA2	1.307548	0.0454466
ENSCAFG00000012963		2.646114	0.0005253
ENSCAFG00000012979	CABCOCO1	-1.0147807	0.0444818
ENSCAFG00000013006	ITGA6	-1.0897465	0.0499311
ENSCAFG00000013020	STMN3	1.7524345	0.0090174

ENSCAFG00000013030	PDHA1	-1.2582977	0.0064577
ENSCAFG00000013042	MYOM3	1.4743933	0.0107657
ENSCAFG00000013098	ZNF750	-1.956704	0.0054493
ENSCAFG00000013195	EFEMP2	1.5427688	0.0004771
ENSCAFG00000013198	FAM234B	1.0223832	0.0104746
ENSCAFG00000013199		1.0030748	0.0475596
ENSCAFG00000013260	KLHL34	1.1853515	0.0382216
ENSCAFG00000013283	CHRNA1	2.9606093	6.85E-06
ENSCAFG00000013367	HIP1	1.4075213	1.33E-06
ENSCAFG00000013423	FUOM	-1.0463725	0.0446137
ENSCAFG00000013483	TMEM120A	-1.0259625	0.045893
ENSCAFG00000013489	UCK2	1.4569271	0.0002208
ENSCAFG00000013500	LTBP3	1.6657797	1.25E-05
ENSCAFG00000013521	POLA1	1.0773683	0.0009952
ENSCAFG00000013544	HSPB1	1.0103984	0.0017707
ENSCAFG00000013600	PTH1R	1.904094	0.0158524
ENSCAFG00000013627	HHIPL2	-1.4953735	0.0344696
ENSCAFG00000013723	SHF	2.4715009	0.0493235
ENSCAFG00000013728	MYL4	1.7469811	0.0369631
ENSCAFG00000013735	ITGB3	1.3294749	0.0442336
ENSCAFG00000013765	MYL10	1.7510174	0.0295485
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ENSCAFG00000013819	FMNL1	1.1166418	0.0161139
ENSCAFG00000013844	NCAM1	2.9879962	0.0014817
ENSCAFG00000013874	CXCR6	-1.5894894	0.0050372
ENSCAFG00000013904	BCL6	1.1057104	0.0013396
ENSCAFG00000013909	SERPINE1	2.1188311	0.006915
ENSCAFG00000013990		1.0084104	0.0189195
ENSCAFG00000014016	DLAT	-1.3390803	0.0038942
ENSCAFG00000014025	TTN	1.4445079	0.0119511
ENSCAFG00000014049	CLEC3B	1.4917439	0.0312897
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ENSCAFG00000014120		1.0228138	0.0055869
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ENSCAFG00000014237	L2HGDH	-1.5465101	0.0003665
ENSCAFG00000014308	ALAS2	1.5514593	0.0001249
ENSCAFG00000014310	APEX2	1.5301556	0.0001018
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ENSCAFG00000014451	MAOB	-4.1786538	4.33E-07
ENSCAFG00000014453	AFAP1	1.0634352	0.0181045
ENSCAFG00000014474	IGFBP5	2.0624697	0.0058444
ENSCAFG00000014490	IGFBP2	4.0896174	0.0028689
ENSCAFG00000014529	CENPL	1.4391555	0.0116044
ENSCAFG00000014551	GAL3ST4	1.7826514	0.0234653
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ENSCAFG00000014627		1.1761091	0.0041188

ENSCAFG00000014777	RCOR2	2.0924226	0.0064773
ENSCAFG00000014812	COL3A1	1.7284213	0.0230001
ENSCAFG00000014835	USP54	1.4163658	0.0445425
ENSCAFG00000014923	FGF7	2.8722276	0.0068474
ENSCAFG00000014968		1.5405599	1.72E-06
ENSCAFG00000014978		1.5139895	0.0001429
ENSCAFG00000015013	LGALS3	1.4125828	0.0318277
ENSCAFG00000015027	METTL11B	-2.0559084	0.0107291
ENSCAFG00000015078	FAM184B	2.424281	0.0008864
ENSCAFG00000015196	SCNN1A	1.5036275	0.0333578
ENSCAFG00000015209	TUBA4A	-1.5157688	0.0215853
ENSCAFG00000015217		-1.6895544	0.0139284
ENSCAFG00000015235	SLC19A2	-1.0788877	0.0153086
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ENSCAFG00000015345	CC2D2A	1.0004909	0.0264898
ENSCAFG00000015372	CPEB2	-1.0892319	0.0116984
ENSCAFG00000015455	ECT2	1.4983674	0.0064693
ENSCAFG00000015484	WSCD1	-2.1157461	0.0063044
ENSCAFG00000015539	PAX7	1.4949196	0.0151456
ENSCAFG00000015550		1.6064299	0.0060471
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ENSCAFG00000015918	RAB31L1	1.3988076	0.0213654
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ENSCAFG00000016072		1.6673666	0.0149674
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ENSCAFG00000016338	KAZN	2.1394648	0.0024173
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ENSCAFG00000016423	PIGH	-1.1379221	0.0015057
ENSCAFG00000016465	MAGED2	1.0708573	0.0069458
ENSCAFG00000016479	TMEM184A	-2.8310203	0.0019848
ENSCAFG00000016550	ASB12	-1.1813558	0.0338087
ENSCAFG00000016615	MRI1	1.1243049	0.0157275
ENSCAFG00000016679	MAP3K9	-2.1018381	1.37E-05
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ENSCAFG00000016811	RHBG	-1.2139594	0.0390907
ENSCAFG00000016828	COPZ2	1.55606	9.93E-05
ENSCAFG00000017018	COL1A1	2.1820931	0.0051535
ENSCAFG00000017024	ZC2HC1C	-1.0476075	0.004418
ENSCAFG00000017033	EME1	1.531999	0.0211695
ENSCAFG00000017050	ACSF2	1.4978868	0.0309289
ENSCAFG00000017080	EPN3	1.6601416	0.0087207
ENSCAFG00000017112	SPG21	1.0279531	0.0008303
ENSCAFG00000017125		-1.4548424	0.0059763
ENSCAFG00000017157	HDAC8	1.0553816	0.0005174
ENSCAFG00000017160	IGDCC4	1.1793074	0.0014497
ENSCAFG00000017262	MYH10	1.7261126	0.0236976
ENSCAFG00000017326		2.7536982	0.0293583
ENSCAFG00000017329	FLRT2	1.2105097	0.0025166
ENSCAFG00000017397	ZNF711	2.0527961	0.0007113
ENSCAFG00000017428	SWSAP1	1.792016	0.0207625
ENSCAFG00000017478	TTC8	1.1792995	0.0118093
ENSCAFG00000017484	CYFIP2	1.4170584	0.0264051
ENSCAFG00000017493	TSPOAP1	1.1371426	0.0311239
ENSCAFG00000017550	S100A4	2.1240684	0.0358078
ENSCAFG00000017553	S100A6	1.5117525	0.0044401
ENSCAFG00000017557	S100A8	2.6007141	0.0045293
ENSCAFG00000017575	MYH4	-1.7587674	0.0357635
ENSCAFG00000017612	ASB2	-1.1992848	0.0001212
ENSCAFG00000017615	ST8SIA5	-1.110632	0.0058133
ENSCAFG00000017616	LARP6	1.6476799	0.0141807
ENSCAFG00000017623	LRRC49	1.5510622	0.0235205
ENSCAFG00000017655		-1.2403254	0.0147905
ENSCAFG00000017702	ARMCX6	2.1443514	6.07E-05
ENSCAFG00000017705	ARMCX2	2.4298609	5.15E-05
ENSCAFG00000017774	ARMCX5	1.2952388	0.0193136
ENSCAFG00000017820	CD276	1.2141377	0.0053039
ENSCAFG00000017823		-1.3003938	0.0168346
ENSCAFG00000017883	NRK	5.0184123	3.84E-05
ENSCAFG00000017889	EVL	1.0430067	0.0034213
ENSCAFG00000017931	RNF128	-1.5185238	0.0010198
ENSCAFG00000017937	CYP1A1	-3.905976	0.0006994
ENSCAFG00000018005	MAN2C1	1.091192	0.0006648
ENSCAFG00000018017	RNF138	-1.0593869	0.0255011
ENSCAFG00000018020	COL4A5	2.1538485	0.0178569
ENSCAFG00000018027	GPRC5B	-1.3592749	1.75E-05
ENSCAFG00000018047		2.4537473	0.0013029
ENSCAFG00000018051	DSG2	1.0198546	0.0496081
ENSCAFG00000018125	AQP4	-2.2918826	0.0138088
ENSCAFG00000018127	TMC7	1.3249101	0.039771
ENSCAFG00000018173	LAMA3	-1.2667093	0.0360097
ENSCAFG00000018175	CAPN6	2.1028427	3.67E-06
ENSCAFG00000018194		2.008607	0.0026407

ENSCAFG00000018272	KLHL13	1.0241092	0.0180757
ENSCAFG00000018277		2.127095	0.002478
ENSCAFG00000018314	CD209	2.5268014	0.0160053
ENSCAFG00000018360		4.5329804	9.56E-05
ENSCAFG00000018405	FST	2.4748204	0.0012487
ENSCAFG00000018415	MOCS2	-1.0281283	0.0311253
ENSCAFG00000018457	NT5M	-1.9198135	0.0039645
ENSCAFG00000018511		1.2177671	0.0498374
ENSCAFG00000018560	MYH11	1.9569557	0.0313494
ENSCAFG00000018576	NIM1K	-3.6134555	0.0314474
ENSCAFG00000018586		1.1431839	0.0023519
ENSCAFG00000018602	SH2D3A	-1.512252	0.0362645
ENSCAFG00000018621	CACHD1	1.4397581	0.0034935
ENSCAFG00000018629	WSB1	1.0999997	0.0083139
ENSCAFG00000018643	SLC25A23	2.1966473	0.0015464
ENSCAFG00000018661	LIFR	-1.2735578	0.0095799
ENSCAFG00000018670	PGM1	-1.1011143	0.0283704
ENSCAFG00000018673	SMARCA1	1.0045601	0.0019892
ENSCAFG00000018702	EFCAB7	-2.4450627	0.0003251
ENSCAFG00000018704	SLC1A3	-1.8758384	0.0117275
ENSCAFG00000018761	PIEZO2	2.0808526	0.0480345
ENSCAFG00000018785	ARHGAP36	2.1698577	0.0347071
ENSCAFG00000018825		2.3704429	0.0029332
ENSCAFG00000018832	TUBB6	1.0036915	0.0087306
ENSCAFG00000018864	GPC3	2.0093935	0.0159679
ENSCAFG00000018873		-1.3988726	0.0304302
ENSCAFG00000018959	EMP2	1.1732602	0.0012158
ENSCAFG00000018982	MYO5B	-1.5390049	0.0131695
ENSCAFG00000019014	SEMA6B	2.0486197	0.0005613
ENSCAFG00000019132	RPH3AL	-1.331736	0.0394341
ENSCAFG00000019134	PPL	1.3445513	0.0350349
ENSCAFG00000019166	ROGDI	-2.2268224	0.0014886
ENSCAFG00000019176	ZNF185	1.6260798	0.0483279
ENSCAFG00000019177	SLC1A7	1.3475283	0.0410859
ENSCAFG00000019183	PODN	1.1923539	0.0428267
ENSCAFG00000019189	BGN	2.3303051	0.001354
ENSCAFG00000019230	ATP2B3	1.7097685	0.0488578
ENSCAFG00000019242	PNCK	-2.0762739	0.0240895
ENSCAFG00000019377	CAMKK1	2.1178586	0.0004866
ENSCAFG00000019401	PGP	-1.0041762	0.0003175
ENSCAFG00000019479		1.1048443	0.0226916
ENSCAFG00000019489	TP73	2.5996216	0.0011885
ENSCAFG00000019541	TRAF2	1.1306474	0.0010248
ENSCAFG00000019601	SOX8	2.508841	6.49E-05
ENSCAFG00000019662	PIGQ	1.3793072	0.0073281
ENSCAFG00000019694	GPSM1	1.7453234	0.0001708
ENSCAFG00000019698	PALM	1.0935731	0.0160607
ENSCAFG00000019714	SLC2A5	3.0560386	0.0366847
ENSCAFG00000019719	TPGS1	1.0672361	0.0123473
ENSCAFG00000019729	MIER2	1.0058426	0.0075446

ENSCAFG00000019764	DENND2D	-1.1679023	0.0347351
ENSCAFG00000019794	SARDH	1.6664619	0.0058041
ENSCAFG00000019837	MYBPHL	-2.4319198	0.0120532
ENSCAFG00000019848	COL5A1	1.5319236	0.0149272
ENSCAFG00000019852	CBFA2T3	1.7435625	3.81E-05
ENSCAFG00000019902	RAPGEF1	-1.0223041	0.0001979
ENSCAFG00000019914		-1.1392902	0.0206516
ENSCAFG00000019956	WFDC1	2.0840362	0.0128731
ENSCAFG00000019964	DNAAF1	-2.5300487	0.0161126
ENSCAFG00000019998	SLC30A7	1.3465529	0.0144063
ENSCAFG00000020004	VCAM1	1.4868283	0.0086088
ENSCAFG00000020024	DYNLRB2	2.0593855	0.0218078
ENSCAFG00000020110	F3	1.3966068	0.0252582
ENSCAFG00000020133	BCAR3	1.383005	0.0032513
ENSCAFG00000020144	FUK	1.0334578	0.0039397
ENSCAFG00000020145		-1.4896673	0.0291662
ENSCAFG00000020153	MTSS1L	1.5078105	0.0005418
ENSCAFG00000020166	ANGPTL2	2.6370734	3.37E-08
ENSCAFG00000020256	ODF2L	1.4931876	0.0062113
ENSCAFG00000020270	COL24A1	3.3611464	0.0003387
ENSCAFG00000020294	HAS3	-2.180502	0.0047527
ENSCAFG00000020304	SSX2IP	1.3445015	0.0003108
ENSCAFG00000020345	PTGFR	-2.7532282	0.0023044
ENSCAFG00000020413	CDH5	-1.3855965	0.026379
ENSCAFG00000020633	cfa-mir-133a	1.1614569	0.0034251
ENSCAFG00000020713	RF00279	-1.6847085	0.0003797
ENSCAFG00000021575	RF00100	4.0455491	0.0071943
ENSCAFG00000021919	RF00100	4.2425627	0.0022207
ENSCAFG00000021953	RF00100	3.8509152	0.0066893
ENSCAFG00000022010	RF00100	4.0197572	0.0022227
ENSCAFG00000022297	RF00012	2.9367081	0.0100984
ENSCAFG00000022574	RF00100	4.6652664	0.0021845
ENSCAFG00000022720		1.4363181	0.0103548
ENSCAFG00000022721		1.3919904	0.0212696
ENSCAFG00000022843	MIR675	3.9588961	3.01E-05
ENSCAFG00000023022		-1.2549395	0.0068233
ENSCAFG00000023094	MYH3	1.7453169	0.0001939
ENSCAFG00000023313		2.1944873	0.0333169
ENSCAFG00000023339		-1.1525263	0.0132799
ENSCAFG00000023755	GMPPB	1.1331362	0.0275096
ENSCAFG00000023757	ADAMTSL2	1.8139829	0.0251371
ENSCAFG00000023759	MT2A	3.3656166	0.0001174
ENSCAFG00000023881	ZNF227	1.3708991	0.0086881
ENSCAFG00000023887	BCAS4	1.8259834	0.0146779
ENSCAFG00000023904	CHRN4	2.2639691	0.0099671
ENSCAFG00000023986	TMEM121	1.9995846	0.0163271
ENSCAFG00000024187	DPEP2	-1.4942701	0.0274082
ENSCAFG00000024239	MLLT11	2.9445566	0.0004494
ENSCAFG00000024609	CNTN2	2.1734298	0.0011631
ENSCAFG00000024681		3.5540753	0.000546

ENSCAFG00000024731	RP9	-1.0923094	0.001598
ENSCAFG00000024802		1.0538697	0.0490096
ENSCAFG00000024807	CHRNA	6.4101752	0.0001536
ENSCAFG00000024834		2.6919239	0.0140258
ENSCAFG00000024901	ZSCAN12	-1.1339625	0.0057243
ENSCAFG00000024908	PLA2G4E	2.8758367	0.001596
ENSCAFG00000025020		1.005517	0.0481236
ENSCAFG00000025213	FAM111B	1.1300711	0.0132696
ENSCAFG00000025295		1.1393788	0.0006477
ENSCAFG00000025390	SLC22A17	2.0374905	7.29E-05
ENSCAFG00000025473	CPA4	1.2926093	0.0043027
ENSCAFG00000025524		1.0511327	0.0114232
ENSCAFG00000025555		-2.6909253	0.016625
ENSCAFG00000025589		-1.117152	0.0461707
ENSCAFG00000025678	cfa-mir-568	1.0256103	0.0434385
ENSCAFG00000027573		2.4892775	3.81E-05
ENSCAFG00000027890	RF00002	2.2516003	0.0133556
ENSCAFG00000028220	RF00009	5.1149746	0.000296
ENSCAFG00000028459	MT3	2.8744037	0.0004428
ENSCAFG00000028460		2.3652681	0.0011151
ENSCAFG00000028490		1.7891883	0.0322275
ENSCAFG00000028544		2.6257845	0.0080108
ENSCAFG00000028594	RF01973	3.7917289	3.18E-05
ENSCAFG00000028636	IGFBP6	1.3041374	0.0212964
ENSCAFG00000028647	BGLAP	2.2628671	0.0037027
ENSCAFG00000028653		1.907295	0.0059677
ENSCAFG00000028708	SCD5	-1.3344739	0.04675
ENSCAFG00000028739	ABHD10	-1.2262447	0.0085553
ENSCAFG00000028748		3.3619939	0.0029589
ENSCAFG00000028753	RF00001	2.6811898	0.0361246
ENSCAFG00000028761		1.3584144	0.0487441
ENSCAFG00000028802	MRPL34	-1.1449448	0.0002084
ENSCAFG00000028808		1.4620694	0.0027875
ENSCAFG00000028817	CFD	1.3802115	0.013706
ENSCAFG00000028869	GPX8	1.1557273	0.010241
ENSCAFG00000028877		-1.1322645	0.0240401
ENSCAFG00000028947	ELN	1.8641504	0.0049252
ENSCAFG00000028958	TCEAL7	3.7209306	0.0001178
ENSCAFG00000028982		1.3853987	0.0432197
ENSCAFG00000028987		3.5433383	0.0015061
ENSCAFG00000029004		-1.2820236	0.0002613
ENSCAFG00000029079	ZNF614	1.0374636	0.0172793
ENSCAFG00000029129	RF01871	3.54521	1.28E-05
ENSCAFG00000029130	KAZALD1	2.0050846	0.005158
ENSCAFG00000029153	PEG3	1.0453331	0.0092147
ENSCAFG00000029304	RF01972	4.2701575	7.95E-06
ENSCAFG00000029322	SCN2B	2.4707413	0.0060704
ENSCAFG00000029324		1.0206873	0.0478012
ENSCAFG00000029369		2.8714409	0.0040285
ENSCAFG00000029381		1.3972429	0.0207192

ENSCAFG00000029384		2.6621783	0.0084145
ENSCAFG00000029474	GADD45A	1.409163	0.0013478
ENSCAFG00000029499		3.1489717	0.0119107
ENSCAFG00000029502		1.2176111	0.0071638
ENSCAFG00000029512		2.7447172	0.0180189
ENSCAFG00000029612	MSS51	-1.8274801	0.0435307
ENSCAFG00000029657		2.9692702	0.0074776
ENSCAFG00000029673		1.4969374	0.0002389
ENSCAFG00000029853	CDKN1A	2.9091499	1.35E-06
ENSCAFG00000029856	RF01881	8.0200698	0.0200494
ENSCAFG00000029882	MISP	5.1712415	1.65E-06
ENSCAFG00000029937	EFHD1	2.3529143	0.0011461
ENSCAFG00000030004	COA7	-1.0688607	8.85E-05
ENSCAFG00000030025	FGL2	1.641265	0.0002306
ENSCAFG00000030105	IL33	1.4345488	0.0422877
ENSCAFG00000030120	CSPG4	2.7799717	0.0005772
ENSCAFG00000030140		2.8599576	0.0057306
ENSCAFG00000030170	ZNF229	1.1313469	0.0487053
ENSCAFG00000030198		2.0380779	0.0270569
ENSCAFG00000030205	KCTD1	1.109113	0.0247439
ENSCAFG00000030240	DUSP4	1.01176	0.0194178
ENSCAFG00000030242	HS3ST2	1.5293694	0.0011212
ENSCAFG00000030310		1.5452991	0.0099306
ENSCAFG00000030348		-1.2217618	0.0010206
ENSCAFG00000030356		1.1828407	0.0262119
ENSCAFG00000030412	BCL2L11	1.2916706	0.0367189
ENSCAFG00000030416	RGS16	-1.1745519	0.0106075
ENSCAFG00000030425		-1.3599376	0.0177819
ENSCAFG00000030469		3.9851279	0.0003344
ENSCAFG00000030538		-1.1587034	0.0403714
ENSCAFG00000030576	PPP1R15A	1.2488683	0.0080266
ENSCAFG00000030616		3.2498502	0.0042798
ENSCAFG00000030655		4.2787272	0.0008717
ENSCAFG00000030662		1.7734667	0.0204471
ENSCAFG00000030667		1.3199661	0.0078169
ENSCAFG00000030670		1.0237026	0.0178795
ENSCAFG00000030686	GLIPR2	1.3445222	0.0158092
ENSCAFG00000030757		1.0113553	0.0373816
ENSCAFG00000030770		2.106183	2.52E-05
ENSCAFG00000030835		-1.2894461	0.0031047
ENSCAFG00000030867	HPCAL4	-1.7995289	0.001087
ENSCAFG00000030875		2.1590787	0.0074889
ENSCAFG00000030932	TMEM218	2.1827057	0.000795
ENSCAFG00000031172	CADM4	1.0076534	0.010747
ENSCAFG00000031239		1.5317568	0.0189766
ENSCAFG00000031281		3.1999672	0.000871
ENSCAFG00000031299		1.5004841	0.0012285
ENSCAFG00000031302		1.2318253	0.0035419
ENSCAFG00000031337		1.2002897	0.0428143
ENSCAFG00000031392	PRR7	1.4726677	0.0108541

ENSCAFG00000031481		-2.0915967	0.0043924
ENSCAFG00000031490		2.8652406	0.0067246
ENSCAFG00000031499	GLIS3	2.0046546	0.0270222
ENSCAFG00000031514		2.9934354	0.0035361
ENSCAFG00000031544		1.9944877	0.0185174
ENSCAFG00000031706		-1.2258907	0.048265
ENSCAFG00000031727	STC2	1.6863172	0.0114515
ENSCAFG00000031759	NAPRT	1.1033874	0.0289729
ENSCAFG00000031894	TENT5A	1.227333	0.0367399
ENSCAFG00000031922	GPX3	2.3486299	0.0121651
ENSCAFG00000031936	NRBF2	-1.2288764	0.0170197
ENSCAFG00000031938	GEM	1.6532407	0.023744
ENSCAFG00000032024	GPR162	-2.0269322	0.0187453
ENSCAFG00000032029		1.0383588	0.0189227
ENSCAFG00000032032		-1.3905757	0.0176839
ENSCAFG00000032043		-1.9397272	0.0012097
ENSCAFG00000032089		1.4611743	0.0409852
ENSCAFG00000032112	TAL2	3.649864	0.0110786
ENSCAFG00000032120	C1QTNF6	1.8173234	0.0066008
ENSCAFG00000032147	BAALC	-1.4898624	0.0007005
ENSCAFG00000032163		2.8190653	0.0140401
ENSCAFG00000032167		2.8133738	0.0052328
ENSCAFG00000032191	MAP1A	2.3750453	0.0251785
ENSCAFG00000032214		2.6736124	0.011212
ENSCAFG00000032227	OLFM1	3.3765206	1.23E-05
ENSCAFG00000032235		1.144905	0.0080936
ENSCAFG00000032276		2.9731028	0.004711
ENSCAFG00000032286		1.4669801	0.0147116
ENSCAFG00000032331		3.5397125	0.0049591
ENSCAFG00000032392		1.2463359	0.0002074
ENSCAFG00000032403	MAP3K7CL	1.506873	0.0100996
ENSCAFG00000032443		3.4716236	0.001794
ENSCAFG00000032445		1.8445519	0.0009014
ENSCAFG00000032467		2.9223795	0.0055118
ENSCAFG00000032571		3.4435978	1.44E-05
ENSCAFG00000032572		3.7383654	0.0014285
ENSCAFG00000032575		-1.6026832	0.0070082
ENSCAFG00000032608	LURAP1L	-1.0209278	0.0451573
ENSCAFG00000032684		1.4374918	0.0202985
ENSCAFG00000032696		2.6616931	0.0184259
ENSCAFG00000032697	MAP6D1	-2.2936664	0.0022139
ENSCAFG00000032871		1.913815	0.031141
ENSCAFG00000032896		1.9658944	0.0013117
ENSCAFG00000032925		1.5000178	0.0239158
ENSCAFG00000033011		-2.7498582	0.0199728
ENSCAFG00000033181		1.1039208	0.0017598
ENSCAFG00000033248		-3.8962083	5.12E-05
ENSCAFG00000033312		-1.4508388	0.0116434
ENSCAFG00000033531		2.8653777	0.0060876
ENSCAFG00000033759		-4.1657867	0.0013268

ENSCAFG00000034014	-1.9095631	0.0002254
ENSCAFG00000034213	1.4423746	0.0087016
ENSCAFG00000034661	1.7239482	0.005424
ENSCAFG00000034853	-1.4165901	0.0092611
ENSCAFG00000034881	1.7999213	0.0092183
ENSCAFG00000035036	-1.834187	0.0248834
ENSCAFG00000035199	3.6010681	0.000318
ENSCAFG00000035602	1.5694818	0.0240247
ENSCAFG00000035834	-2.5156096	0.0154571
ENSCAFG00000036044	1.9723707	0.040506
ENSCAFG00000036200	-1.4070921	0.0179547
ENSCAFG00000036350	-2.584086	0.0416305
ENSCAFG00000036996	1.4684042	0.006014
ENSCAFG00000037515	1.3333519	0.0081007
ENSCAFG00000037835	-2.0754566	0.0096627
ENSCAFG00000037878	-2.6736902	1.93E-06
ENSCAFG00000038197	1.507816	0.0363727
ENSCAFG00000038302	2.9220076	0.0050989
ENSCAFG00000038320	-2.4808233	9.85E-08
ENSCAFG00000038468	3.9072856	0.0002694
ENSCAFG00000038525	-1.0654407	0.0375253
ENSCAFG00000038545	1.693673	0.0123975
ENSCAFG00000038558	3.0831221	0.0001577
ENSCAFG00000038812	-2.0347806	0.038946
ENSCAFG00000039156	-1.0317933	0.0427547
ENSCAFG00000039836	5.0522795	0.0018335
ENSCAFG00000040479	-3.108107	0.0104588
ENSCAFG00000040506	1.8240824	0.0249977
ENSCAFG00000040611	1.651615	0.0362967

Table S3: List of differentially expressed genes in the Vastus lateralis muscle of untreated XLMTM dogs, compared to WT controls; logFC: base 2 logarithm of the expression fold change (XLMTM / WT).

ensembl ID	Gene name	logFC	PValue
ENSCAFG00000000068	BCL2	1.512914721	0.005146778
ENSCAFG00000000082	CDK2	1.172962758	0.012277282
ENSCAFG00000000097	ERBB3	2.836526719	0.003004938
ENSCAFG00000000124	TIMELESS	1.393514773	0.013025503
ENSCAFG00000000235	N4BP3	-1.313344461	0.001392379
ENSCAFG00000000236	RMND5B	-1.048452164	0.001016577
ENSCAFG00000000251	MAP3K5	1.266306896	0.018975459
ENSCAFG00000000282	HECA	-1.116657654	0.000100464
ENSCAFG00000000288		1.225063765	0.014366904
ENSCAFG00000000311	LRIG3	1.300635589	0.035351857
ENSCAFG00000000330	FBXO30	1.052853722	0.008727095
ENSCAFG00000000420	CPM	2.721416191	0.000992424
ENSCAFG00000000426	LYZ	-1.27603093	1.00E-05
ENSCAFG00000000448	DDR1	1.154792529	0.030021316
ENSCAFG00000000456	THAP2	-1.029351568	0.003465968
ENSCAFG00000000479	KCNC2	1.198295396	0.019905426
ENSCAFG00000000493	OSR2	1.592400768	0.005010673
ENSCAFG00000000510	PRR16	3.965700458	2.68E-07
ENSCAFG00000000522	SNCAIP	-1.248719196	0.005918512
ENSCAFG00000000523		1.27777025	0.003421019
ENSCAFG00000000535	MYCT1	-1.542886278	6.70E-05
ENSCAFG00000000565		1.142983473	0.011662693
ENSCAFG00000000568	MAPK8IP2	1.044702044	0.026063634
ENSCAFG00000000569	ZNF608	1.1270997	0.00171455
ENSCAFG00000000594	MARCH3	1.044053623	0.047267013
ENSCAFG00000000611	MEGF10	1.239697597	0.001356059
ENSCAFG00000000622	PRRC1	1.158353573	0.001115949
ENSCAFG00000000626		1.118519336	0.003150302
ENSCAFG00000000639	HSPA1L	-1.016924772	0.000512148
ENSCAFG00000000640		-1.387721827	0.008899671
ENSCAFG00000000641		-1.361720915	0.011875895
ENSCAFG00000000644	SYNJ2	1.022446966	0.034369308
ENSCAFG00000000654	FZD6	-1.053074181	0.00378533
ENSCAFG00000000667	FNDC1	2.103958151	0.007866071
ENSCAFG00000000671	SOD2	-1.111481233	0.008075719
ENSCAFG00000000701		1.53986253	9.93E-06
ENSCAFG00000000750	SLC22A1	3.041867806	0.018075209
ENSCAFG00000000798		-1.333510837	0.02002046
ENSCAFG00000000840	SLC22A4	1.528584769	0.010455085
ENSCAFG00000000884	WDR27	1.459863864	0.018722658
ENSCAFG00000000886	DSE	1.632552992	7.49E-06
ENSCAFG00000000934	COL14A1	2.085664665	0.000262749
ENSCAFG00000000946	A4GALT	1.17478725	4.82E-05
ENSCAFG00000001023	MEI1	1.010716423	0.041012045
ENSCAFG00000001106	LAMA2	1.964839444	0.006539003
ENSCAFG00000001126	KLHL3	1.302068645	0.015689971

ENSCAFG00000001166	KHDRBS3	1.913245744	0.003910825
ENSCAFG00000001176	MRPL55	-1.012312936	0.010033826
ENSCAFG00000001250	MROH5	2.312570414	0.018277086
ENSCAFG00000001287	TCP11	-2.03217957	0.000182647
ENSCAFG00000001299	ZC3H3	1.125862995	0.038769959
ENSCAFG00000001317	EEF1D	-1.33016626	0.000415693
ENSCAFG00000001324	ATF4	-1.420750897	0.00129299
ENSCAFG00000001336	ISCA1	-1.007809986	0.000626821
ENSCAFG00000001426	COPG2	1.131063216	3.89E-05
ENSCAFG00000001438	PI16	1.545078912	0.024936228
ENSCAFG00000001453	RASEF	-2.146153007	0.000103851
ENSCAFG00000001513	KCTD17	-1.568934667	6.95E-05
ENSCAFG00000001515	STRIP2	1.255825654	0.000840832
ENSCAFG00000001531	SMO	1.110486728	0.024652808
ENSCAFG00000001537	FREM1	1.621795963	0.004323272
ENSCAFG00000001556	KCNK17	2.305177845	7.20E-05
ENSCAFG00000001596	FOXP4	2.091095449	3.82E-06
ENSCAFG00000001616	KCP	1.85721633	0.00185992
ENSCAFG00000001636	PPP1R16A	1.031576931	0.000870891
ENSCAFG00000001646	PRUNE2	3.399318155	0.000239015
ENSCAFG00000001649	GCNT1	3.056173032	0.000239287
ENSCAFG00000001672	LEP	4.763085891	0.000210633
ENSCAFG00000001705	MB	-1.547539764	0.013542253
ENSCAFG00000001730	GCC1	1.077616813	0.002673402
ENSCAFG00000001793	BTBD11	1.551643808	0.00653172
ENSCAFG00000001840	B4GALT1	1.027668154	0.008661043
ENSCAFG00000001852	ADAM22	-1.374857717	0.025736584
ENSCAFG00000001854		-1.952007842	0.035660473
ENSCAFG00000001875	CKAP4	1.148824276	0.026289292
ENSCAFG00000001885	APPL2	1.239516258	0.000839671
ENSCAFG00000001890	MAMDC2	1.277191367	0.01643615
ENSCAFG00000001897	APBA1	1.215066888	0.019191295
ENSCAFG00000001909	KIF24	1.81716916	0.001685762
ENSCAFG00000001923	DNAI1	4.48304296	0.004636016
ENSCAFG00000001966	SH3RF3	-1.927100824	0.002256998
ENSCAFG00000001985		1.039690188	0.003086778
ENSCAFG00000002040	TFPI2	-1.973603952	0.001865922
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ENSCAFG00000002046	GNG11	-1.54744477	1.38E-05
ENSCAFG00000002053	RFX3	1.84761366	0.002658039
ENSCAFG00000002057	PDGFRA	1.118666213	0.040143448
ENSCAFG00000002069	COL1A2	2.925392536	8.69E-05
ENSCAFG00000002079	KDR	-1.497427782	8.46E-05
ENSCAFG00000002084		1.224256255	0.035327292
ENSCAFG00000002098	C10H2orf40	-1.798114852	0.031979336
ENSCAFG00000002105	FHL2	1.817158446	0.044744006
ENSCAFG00000002116	PLGRKT	-1.364684603	1.22E-05
ENSCAFG00000002195	SDHAF3	-1.190357481	0.027855327
ENSCAFG00000002230		-1.660025677	0.001904885
ENSCAFG00000002301	ECM2	1.078459066	0.008406089

ENSCAFG00000002319	KIAA1211L	3.749003388	3.44E-05
ENSCAFG00000002330	IGFBP7	-1.749127525	8.46E-05
ENSCAFG00000002358	VWA3B	1.331704984	0.001510756
ENSCAFG00000002365	TMEM131	1.345509869	0.00024939
ENSCAFG00000002420	MEOX2	-1.358391232	0.002282639
ENSCAFG00000002432	TSPAN13	-1.704681942	7.09E-06
ENSCAFG00000002498	HDAC9	1.059230809	0.007135728
ENSCAFG00000002517		1.346231484	0.001780718
ENSCAFG00000002576	HIVEP3	2.159868089	0.026518024
ENSCAFG00000002606		1.539278061	0.002205048
ENSCAFG00000002635	RDH13	-1.324156386	0.00894479
ENSCAFG00000002645	KCNQ5	1.674362122	5.51E-05
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ENSCAFG00000002701	TFPT	-1.035921803	0.005092193
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ENSCAFG00000002741	MYO6	1.139662194	0.008117135
ENSCAFG00000002748		1.362743224	0.001197956
ENSCAFG00000002753	GPNMB	2.20112516	0.008669705
ENSCAFG00000002814	KCNQ4	1.85384467	0.006646778
ENSCAFG00000002822	LCA5	1.228737831	0.025094462
ENSCAFG00000002830	RIMS3	-3.512294484	1.20E-05
ENSCAFG00000002837	TMEM245	1.096738154	3.62E-05
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ENSCAFG00000002919	EFEMP1	1.429460589	0.013958762
ENSCAFG00000002927	CCDC85A	-1.196861311	0.000163276
ENSCAFG00000002948	HOXA4	1.118026487	0.011069215
ENSCAFG00000002974	FAM71E1	1.844948802	0.005760653
ENSCAFG00000002994	NT5E	1.127540876	0.010707424
ENSCAFG00000003000	PTGR1	1.357704481	0.000917353
ENSCAFG00000003008	C11H9orf84	8.795896607	3.43E-05
ENSCAFG00000003010	UGCG	1.06033919	0.001411574
ENSCAFG00000003087		1.422426202	0.007883458
ENSCAFG00000003096	PM20D2	1.866701978	0.000482124
ENSCAFG00000003097	CRHR2	1.886625788	0.039923614
ENSCAFG00000003105	ANKRD6	2.501267058	5.76E-06
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ENSCAFG00000003233	MEIS1	1.343509195	0.006184263
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ENSCAFG00000003268	ARHGAP25	-1.17964162	0.001913188
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ENSCAFG00000003327	COL27A1	2.318914477	0.018749267
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ENSCAFG00000003411	EZH2	1.050304162	0.006129439
ENSCAFG00000003465	EGFR	1.208179465	0.013419578
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ENSCAFG00000003530		1.771717875	9.60E-06
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ENSCAFG00000003620	RCN3	1.179797714	0.008966859
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ENSCAFG00000003680	MYLK3	4.790505736	3.28E-06
ENSCAFG00000003700	MAML3	1.498025774	0.040190266
ENSCAFG00000003719	RTN4IP1	-1.03819734	0.010600613
ENSCAFG00000003720	NRCAM	4.283879136	3.64E-07
ENSCAFG00000003775	OSR1	2.733224827	6.01E-05
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ENSCAFG00000003804		1.91604871	0.027291532
ENSCAFG00000003810	PPIL6	1.886156161	0.028278525
ENSCAFG00000003816	SMPD2	1.357520695	0.000567919
ENSCAFG00000003824	MICAL1	2.0767653	4.15E-06
ENSCAFG00000003854	WASF1	1.3667595	0.007760034
ENSCAFG00000003887	APOB	3.292067243	0.003179052
ENSCAFG00000003907	BRAF	1.00346522	0.000782651
ENSCAFG00000003941	SPATA6	1.418324303	0.020156672
ENSCAFG00000003942	REV3L	1.02376239	0.000720562
ENSCAFG00000003960	TRAF3IP2	1.576682143	0.044037897
ENSCAFG00000003961	SPHK2	1.195593731	0.000679054
ENSCAFG00000004029	TMEM143	-1.175801443	0.043712144
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ENSCAFG00000004201	SLC1A5	1.802754086	0.018149829
ENSCAFG00000004232	HS6ST1	1.082993043	1.17E-05
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ENSCAFG00000004297	CCDC8	3.386229398	0.001407136
ENSCAFG00000004300	PNMA8A	1.023434874	0.028642719
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ENSCAFG00000004374	SOX9	2.155439117	0.002347172
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ENSCAFG00000004406	FBLN2	1.336998079	0.010147288
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ENSCAFG00000004636	BCAM	1.431501768	0.004542265
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ENSCAFG00000004801	ASB10	-1.42617755	0.025563651
ENSCAFG00000004802	KBTBD6	1.062898207	0.002315397
ENSCAFG00000004820	ITGA9	1.722472476	0.00240463
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ENSCAFG00000005037	KLF5	1.236429367	0.034166191
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ENSCAFG00000005212	FOSL2	1.220354061	0.005349322
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ENSCAFG00000005963	METTL21C	-4.337630234	0.013432947
ENSCAFG00000005965	FOXO1	1.342420559	0.014760008
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ENSCAFG00000006044	TRPC4	1.852366958	0.038224436
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ENSCAFG00000006175	CDC25B	1.356247088	0.010062323
ENSCAFG00000006215	POLE	1.049985134	0.011285828
ENSCAFG00000006231	DCLK1	3.592784876	7.82E-06
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ENSCAFG00000006250	SPRY4	-1.233853027	0.004228894
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ENSCAFG00000006381	SEMA3C	1.038521177	0.008217059
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ENSCAFG00000006559	ITPRIPL1	-1.397851669	0.000138061
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ENSCAFG0000006673	PPP1R3B	1.184983714	0.024626194
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ENSCAFG0000007036	CD22	-1.719470343	0.001095637
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ENSCAFG0000007562	AMPD3	1.849416153	0.01014497
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ENSCAFG0000007626	PIK3R1	1.067000994	0.005057473
ENSCAFG0000007635	CLSTN2	3.207811607	1.16E-05
ENSCAFG0000007651	DTX4	1.542997297	0.016897439
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ENSCAFG0000007742	TFDP2	-1.002106629	0.001754311
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ENSCAFG0000007832	TCF7L1	1.147972872	0.006259848
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ENSCAFG0000007846	GBE1	1.149584014	0.025409592
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ENSCAFG0000007863	ATR	1.088782499	4.59E-05
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ENSCAFG0000007893	RBP4	2.002499185	0.042251832

ENSCAFG0000007935	TRPC1	1.051945866	0.002529282
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ENSCAFG0000008159	PLSCR4	1.298203627	0.015221206
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ENSCAFG0000008295	BTG3	1.295858635	0.025828207
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ENSCAFG0000008309		-1.43440908	0.023136322
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ENSCAFG0000008354	SCARA5	1.430062668	0.012793785
ENSCAFG0000008391	HEY1	-1.008243771	0.018293645
ENSCAFG0000008403		-1.495917373	0.01247696
ENSCAFG0000008408	TPD52	1.207662589	0.014042884
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ENSCAFG0000008471	CCDC142	1.34579187	0.037734356
ENSCAFG0000008477	BLNK	-1.511547355	0.032220078
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ENSCAFG0000008566	GUCY1B1	-1.117284236	0.02654305
ENSCAFG0000008597	ANGPT2	-2.09122585	7.91E-06
ENSCAFG0000008624	STBD1	-1.132732768	0.039550272
ENSCAFG0000008648		-1.585472155	0.004893517
ENSCAFG0000008707	CKMT2	-1.513175637	0.014869607
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ENSCAFG0000008728	TET3	1.074996219	0.020416875
ENSCAFG0000008741	EPHA3	-1.457587703	0.034203901
ENSCAFG0000008755	SRC	1.483256891	0.012127056
ENSCAFG0000008761	CX3CL1	-1.631523824	0.002692642
ENSCAFG0000008786	NNAT	1.385895771	0.017606039
ENSCAFG0000008837	ANXA3	-1.724798275	0.000125438
ENSCAFG0000008942	C18H11orf49	1.771409836	9.50E-06
ENSCAFG0000008977	LRP4	2.637229703	4.82E-08
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ENSCAFG0000009046	TPCN1	1.026898343	0.008569566
ENSCAFG0000009061	SLC8B1	1.213167326	0.004684416
ENSCAFG0000009066	MYOD1	1.704728854	0.029840809

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ENSCAFG0000009110	MT1E	1.684552853	0.022942676
ENSCAFG0000009113		1.662637003	0.048575535
ENSCAFG0000009149	SMIM4	-1.368540285	0.032207007
ENSCAFG0000009232	AMIGO2	1.688808515	0.013372996
ENSCAFG0000009271	CRTAC1	2.277882249	0.002322052
ENSCAFG0000009282	CREB3L1	2.490627371	0.001186478
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ENSCAFG0000009433	BAZ2B	1.077247347	0.01016707
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ENSCAFG0000009596	RUNX1	2.563379593	0.012764049
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ENSCAFG00000010423	COL4A4	2.911724806	3.71E-08
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ENSCAFG00000012013	ANPEP	1.834642459	0.007660245
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ENSCAFG00000012182	TGM1	3.044524665	5.70E-06
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ENSCAFG00000012405	RBM14	1.043224607	0.002512687
ENSCAFG00000012428	HES6	1.36513027	0.041069199
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ENSCAFG00000012558		1.046927218	0.003719884
ENSCAFG00000012619	MGST1	2.512004864	0.03228505
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ENSCAFG00000012661	RFX5	1.075017609	0.002753632
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ENSCAFG00000014668	SLC35F2	-1.328482258	0.028279613
ENSCAFG00000014679	PLEKHH3	1.129808878	0.01225267
ENSCAFG00000014767	SLC9A7	1.569963702	0.002519878
ENSCAFG00000014812	COL3A1	2.592138197	7.42E-05
ENSCAFG00000014831	SH3BP2	1.577286613	0.002440028
ENSCAFG00000014837	COL5A2	1.677984988	0.005884364
ENSCAFG00000014838	GRIA4	1.938506355	0.000341434
ENSCAFG00000014923	FGF7	3.412306098	3.66E-06
ENSCAFG00000014968		1.234764568	0.000249656
ENSCAFG00000014978		2.333590538	1.59E-07
ENSCAFG00000015009	MAST3	1.311285718	0.008373248
ENSCAFG00000015013	LGALS3	1.228948364	0.016134212
ENSCAFG00000015078	FAM184B	2.420010828	7.78E-06
ENSCAFG00000015091	LGALS12	3.211561178	0.000994195
ENSCAFG00000015196	SCNN1A	1.477010439	0.007560579
ENSCAFG00000015203	PLEKHG6	1.354786785	0.031915668
ENSCAFG00000015209	TUBA4A	-2.085553592	2.82E-05
ENSCAFG00000015217		-2.109544247	1.43E-05
ENSCAFG00000015233	PROM1	-1.623183312	0.002747785
ENSCAFG00000015235	SLC19A2	-1.100735424	0.028790754
ENSCAFG00000015257	ANO2	1.879028699	2.00E-06
ENSCAFG00000015272	FGFBP1	-3.536343867	2.28E-05
ENSCAFG00000015298	CD38	-1.182073932	0.006225598
ENSCAFG00000015320	NDUFA9	-1.05069387	0.019828262
ENSCAFG00000015360	GLDN	1.143461561	0.043070378
ENSCAFG00000015427	ZNF503	2.014152001	0.000243553
ENSCAFG00000015430	ABHD8	-1.117610208	0.046438985
ENSCAFG00000015484	WSCD1	-1.438262849	0.001298777

ENSCAFG00000015512	POU2F1	1.13302006	0.029099661
ENSCAFG00000015539	PAX7	1.395532008	0.0013233
ENSCAFG00000015625	FMN2	1.36151607	0.001317236
ENSCAFG00000015662	GNB5	-1.039096649	0.001076432
ENSCAFG00000015695	PRKCH	-1.248484833	0.000306475
ENSCAFG00000015731	ZNF385C	4.692270181	6.99E-06
ENSCAFG00000015788	B4GALNT3	2.636017186	0.010793726
ENSCAFG00000015878	UCHL1	1.546077843	0.005539765
ENSCAFG00000015920	HAP1	5.043410399	7.96E-05
ENSCAFG00000015936	EPHA4	-1.433980184	0.000185468
ENSCAFG00000015943	PRTG	1.444034917	0.016455217
ENSCAFG00000015968	BCL6B	-1.067609199	0.030692266
ENSCAFG00000016022	KLB	2.546535453	0.027548092
ENSCAFG00000016036		7.016258609	0.049101968
ENSCAFG00000016072		1.103191687	0.011734775
ENSCAFG00000016142	TMEM82	1.324093088	0.007983772
ENSCAFG00000016192	SDK1	1.971691982	0.01024194
ENSCAFG00000016225	ACAP1	1.506539113	0.000457593
ENSCAFG00000016298	TMEM102	1.1467289	0.007763606
ENSCAFG00000016338	KAZN	1.219066392	0.02430905
ENSCAFG00000016357	DBN1	1.328042703	0.004904397
ENSCAFG00000016368	PNMT	1.466302323	0.024897178
ENSCAFG00000016410	PLEKHH1	2.73853123	3.36E-05
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ENSCAFG00000016453	ADGRL1	1.307586207	0.046507597
ENSCAFG00000016465	MAGED2	1.263446026	6.26E-05
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ENSCAFG00000016518	FGFR4	1.145955705	0.00945188
ENSCAFG00000016541	ZNF346	1.273397861	2.96E-05
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ENSCAFG00000016590	FBXO2	2.934905735	0.007266281
ENSCAFG00000016596	DISP3	1.705085064	0.000168437
ENSCAFG00000016602	SMOC1	1.299880856	0.038337447
ENSCAFG00000016615	MRI1	1.149782024	0.011404642
ENSCAFG00000016671	CCDC189	1.052591409	0.008436979
ENSCAFG00000016718	HRH2	2.426529023	0.016221075
ENSCAFG00000016736	FBXL19	1.132719552	0.010898339
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ENSCAFG00000016769	NES	1.905412123	0.002378304
ENSCAFG00000016828	COPZ2	1.028632919	0.036360494
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ENSCAFG00000016880	ATP5MC1	-1.290162435	0.015019756
ENSCAFG00000016928	ALOX15B	6.16785603	0.001562234
ENSCAFG00000016983	RAB8B	1.390517014	0.000339427
ENSCAFG00000016984	PER1	1.287908041	0.023896548
ENSCAFG00000017008	AURKB	1.365287459	0.006146469
ENSCAFG00000017015	CTC1	1.105258943	0.000215681
ENSCAFG00000017018	COL1A1	3.968024002	3.71E-05
ENSCAFG00000017050	ACSF2	1.032690896	0.001570815
ENSCAFG00000017064	CHAD	-3.034747298	0.04528591

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ENSCAFG00000017160	IGDCC4	1.611713842	0.000887137
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ENSCAFG00000017184	IL6R	-1.029822456	0.000192596
ENSCAFG00000017221		1.222681832	0.045185421
ENSCAFG00000017296	RNF145	1.226273609	9.04E-05
ENSCAFG00000017329	FLRT2	1.302922919	4.29E-05
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ENSCAFG00000017357	ADAM19	1.226384993	0.013534516
ENSCAFG00000017369	PCTP	-1.117613987	0.033841182
ENSCAFG00000017409	AKAP1	-1.10400603	0.0014909
ENSCAFG00000017428	SWSAP1	1.371982025	0.008409668
ENSCAFG00000017447	IL4R	1.248343849	0.022922305
ENSCAFG00000017464	MKS1	1.260077764	0.000686005
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ENSCAFG00000017616	LARP6	1.362183971	0.003800504
ENSCAFG00000017623	LRRC49	1.198437276	0.023288841
ENSCAFG00000017635	RNF165	1.158703871	0.046442703
ENSCAFG00000017646	SERPINA1	-1.174885668	0.024622457
ENSCAFG00000017705	ARMCX2	2.602599203	9.83E-05
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ENSCAFG00000017807	CRYM	2.825829237	0.031597899
ENSCAFG00000017820	CD276	1.441143737	0.002608374
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ENSCAFG00000017883	NRK	4.56944269	2.99E-09
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ENSCAFG00000018016	COL4A6	1.458823574	0.045189856
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ENSCAFG00000018047		2.160675078	0.016470294
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ENSCAFG00000018197	ABCC6	1.653929939	0.030537908
ENSCAFG00000018238	TIGD6	1.167965054	0.016284621
ENSCAFG00000018254	GREB1L	1.060288136	0.000784847
ENSCAFG00000018272	KLHL13	1.656963535	6.08E-06
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ENSCAFG00000018323	ABLIM3	-1.34203927	5.97E-05
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ENSCAFG00000018422	FBN3	1.265439091	0.015707351
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ENSCAFG00000018527	PRAM1	2.267653354	0.002051124
ENSCAFG00000018556	WDR78	1.068222779	0.019732746
ENSCAFG00000018586		1.2615627	0.011231598
ENSCAFG00000018591	ARHGAP28	1.078779418	0.044040402
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ENSCAFG00000018622	DAB2	1.23392926	0.02486107
ENSCAFG00000018625	C3	1.77318267	0.028217786
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ENSCAFG00000019071	TRARG1	3.411899961	0.01155865
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ENSCAFG00000019343	FLYWCH1	1.076444656	0.014196013
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ENSCAFG00000019567	RNF207	-1.573054	0.018750376
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ENSCAFG00000019760	MED22	-1.003795679	0.002604276
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ENSCAFG00000019928	GSE1	1.019355506	0.011056873
ENSCAFG00000019950	HMCN2	1.4102366	0.014530595
ENSCAFG00000020004	VCAM1	1.173869177	0.009799168
ENSCAFG00000020024	DYNLRB2	2.549179548	0.001473666
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ENSCAFG00000020144	FUK	1.363530793	5.80E-08
ENSCAFG00000020153	MTSS1L	1.737018296	5.57E-06
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ENSCAFG00000020254	NFAT5	1.457593548	0.001338247
ENSCAFG00000020270	COL24A1	2.567528107	0.027077318
ENSCAFG00000020294	HAS3	-1.40053182	0.000946821
ENSCAFG00000020333	PSMB10	-1.066807478	0.024860678
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ENSCAFG00000025524		2.074208752	0.006384599
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ENSCAFG00000028506		2.666777618	0.000629504
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ENSCAFG00000029321	WNT5A	1.351539574	0.004451194
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ENSCAFG00000029427		1.124815545	0.028043853
ENSCAFG00000029464	CDC34	-1.192289701	0.011546037
ENSCAFG00000029474	GADD45A	1.924300999	3.16E-08
ENSCAFG00000029558	BMF	1.303865998	0.00263344
ENSCAFG00000029587		-1.426038611	0.039437274
ENSCAFG00000029672		-1.292002834	0.010020094
ENSCAFG00000029674		1.110569044	0.000527864
ENSCAFG00000029771	ETFRF1	-1.066628869	0.047038849
ENSCAFG00000029798	RF01955	2.088740867	0.000595944
ENSCAFG00000029853	CDKN1A	2.880122608	3.50E-05
ENSCAFG00000029856	RF01881	10.4738747	0.020926299
ENSCAFG00000029882	MISP	2.717892814	0.010353504
ENSCAFG00000029937	EFHD1	2.224916162	2.69E-05
ENSCAFG00000029969	RGS4	-1.026160719	0.0297151
ENSCAFG00000030025	FGL2	1.646365038	0.006467272
ENSCAFG00000030039		-1.129461395	0.015693099
ENSCAFG00000030057	ZNF234	1.10813289	0.001150161
ENSCAFG00000030058	ECI1	-1.030053819	0.024263669
ENSCAFG00000030080		1.148181614	0.00489728
ENSCAFG00000030091		-1.275913261	0.010161037
ENSCAFG00000030120	CSPG4	2.24944815	0.032928671
ENSCAFG00000030143		-1.066056007	0.012778784

ENSCAFG00000030159		-1.227600944	0.043413381
ENSCAFG00000030198		2.498094202	0.001063778
ENSCAFG00000030307		1.658890403	0.004582828
ENSCAFG00000030320	SHISA2	2.197868448	6.20E-06
ENSCAFG00000030348		-1.296446626	0.004574621
ENSCAFG00000030445		2.000548028	0.000527698
ENSCAFG00000030466		-1.240887145	0.00556606
ENSCAFG00000030529		1.46912927	0.002699317
ENSCAFG00000030538		-1.075435722	0.013442398
ENSCAFG00000030588		2.723270352	0.001089448
ENSCAFG00000030617	NXP3	-2.561698096	0.025531412
ENSCAFG00000030662		3.778100823	1.11E-05
ENSCAFG00000030682		3.481809075	4.97E-05
ENSCAFG00000030715		1.765640989	0.000114114
ENSCAFG00000030745	SRSF12	1.108425678	0.01475907
ENSCAFG00000030769	SLC35F6	1.193279372	0.005878154
ENSCAFG00000030770		1.930142258	0.015083311
ENSCAFG00000030835		-1.451368233	0.017367549
ENSCAFG00000030838	PTGES	2.013018561	0.016653489
ENSCAFG00000030871		1.05857212	0.007375821
ENSCAFG00000030875		1.608460075	0.048815124
ENSCAFG00000030921	ATP5MD	-1.059311162	0.033068031
ENSCAFG00000030932	TMEM218	1.366326812	0.002125813
ENSCAFG00000030939		1.528769482	0.002116392
ENSCAFG00000030990	INSYN1	-1.061935662	0.022583191
ENSCAFG00000030999		1.52685938	0.005710941
ENSCAFG00000031042	PLAGL2	1.246297526	0.013784998
ENSCAFG00000031124	APH1B	1.00076677	0.026136988
ENSCAFG00000031158	EPDR1	-1.118055986	0.049551727
ENSCAFG00000031234	KY	1.815304444	6.53E-06
ENSCAFG00000031239		3.005095626	0.000570039
ENSCAFG00000031288	RF01956	1.827918233	0.002792908
ENSCAFG00000031322	PDXK	1.305125294	0.001498442
ENSCAFG00000031328	RF01956	2.367910209	0.002575286
ENSCAFG00000031376	UBXN2A	-1.177242351	0.002420848
ENSCAFG00000031437		1.919612134	0.010516873
ENSCAFG00000031454		1.094919979	0.027078429
ENSCAFG00000031481		-3.618944662	0.001123586
ENSCAFG00000031536	LDLRAD4	-1.135538343	0.036520225
ENSCAFG00000031544		1.157752637	0.046680847
ENSCAFG00000031557		1.502635768	0.000783021
ENSCAFG00000031576	PARD6A	-1.317161772	0.015439296
ENSCAFG00000031628		-1.048957844	0.011287982
ENSCAFG00000031672	CLBA1	1.385946391	0.009493958
ENSCAFG00000031678	POLR2M	-1.078491234	0.002957049
ENSCAFG00000031706		-1.28177841	0.000149951
ENSCAFG00000031711		-1.031745791	0.007657675
ENSCAFG00000031732		1.208240735	0.023597593
ENSCAFG00000031759	NAPRT	1.137586726	0.000246641
ENSCAFG00000031761	NDUFAF4	-1.157022869	0.00342678

ENSCAFG00000031767	TUBA3D	-1.183800581	0.008601769
ENSCAFG00000031894	TENT5A	1.583488798	0.007734554
ENSCAFG00000031936	NRBF2	-1.185641603	0.003078252
ENSCAFG00000031973		1.332445171	0.006817586
ENSCAFG00000032024	GPR162	-2.463949496	6.21E-05
ENSCAFG00000032043		-2.20433237	0.001678703
ENSCAFG00000032112	TAL2	2.94392871	0.004917625
ENSCAFG00000032118		-1.138895773	0.018276892
ENSCAFG00000032120	C1QTNF6	2.399081358	0.000135655
ENSCAFG00000032127	CHST11	2.345499067	6.03E-05
ENSCAFG00000032147	BAALC	-1.13266298	0.002420569
ENSCAFG00000032192	RF01957	1.877600911	0.001393978
ENSCAFG00000032227	OLFM1	2.018599342	0.001343614
ENSCAFG00000032235		1.063675433	0.022272439
ENSCAFG00000032261	SPA17	1.15161096	0.006804599
ENSCAFG00000032271	CLEC2L	-2.673159068	0.010646838
ENSCAFG00000032273	FXVD6	-1.02034559	0.004449233
ENSCAFG00000032286		3.21861502	0.000368607
ENSCAFG00000032289	BMP6	-1.032987354	0.000296286
ENSCAFG00000032331		3.759854124	0.00023202
ENSCAFG00000032339	CYP2A13	3.901819907	0.003396964
ENSCAFG00000032342	PDGFD	1.400444854	0.020132685
ENSCAFG00000032355		-1.009631633	0.003177971
ENSCAFG00000032379	PEG10	1.896958064	0.015761427
ENSCAFG00000032391	FAM83H	2.867942717	5.20E-05
ENSCAFG00000032403	MAP3K7CL	2.373587607	0.000262929
ENSCAFG00000032412	FLI1	-1.077108936	0.008566654
ENSCAFG00000032457	MAFA	1.080659691	0.006458248
ENSCAFG00000032459		-1.283411154	0.004252818
ENSCAFG00000032489	SHISA7	1.212888972	0.03862263
ENSCAFG00000032569	RBP1	-1.768499041	0.02438051
ENSCAFG00000032571		3.739198549	1.03E-05
ENSCAFG00000032575		-1.078791495	0.030479117
ENSCAFG00000032578		6.30787986	0.000471961
ENSCAFG00000032608	LURAP1L	-1.145101363	0.004169693
ENSCAFG00000032656		1.339257263	0.001295681
ENSCAFG00000032684		3.042024837	0.000473205
ENSCAFG00000032694	TFB2M	-1.275430636	0.000734926
ENSCAFG00000032756	FAM198B	-1.064271179	0.007440683
ENSCAFG00000032816		1.215080564	0.01315781
ENSCAFG00000032896		2.943493356	2.03E-05
ENSCAFG00000032930		1.677166808	0.00614993
ENSCAFG00000033011		-2.743409349	0.015945439
ENSCAFG00000033086		2.931779724	0.014295762
ENSCAFG00000033248		-3.429665114	6.00E-05
ENSCAFG00000033312		-1.936984845	0.000720157
ENSCAFG00000033759		-4.107143429	6.77E-05
ENSCAFG00000034559		-1.025799586	0.01361523
ENSCAFG00000034578		-1.802512961	0.027193228
ENSCAFG00000034881		2.008075137	0.003050977

ENSCAFG00000034998	-1.43732112	0.00348454
ENSCAFG00000035036	-1.682876794	0.019500818
ENSCAFG00000035090	-1.006349504	0.008010664
ENSCAFG00000035199	2.07300263	0.010484605
ENSCAFG00000035325	-2.093413811	0.000590218
ENSCAFG00000035481	-1.381384111	0.034922837
ENSCAFG00000036055	1.535277971	0.005403628
ENSCAFG00000036094	-1.043466658	0.01636768
ENSCAFG00000037282	3.739182512	0.00035113
ENSCAFG00000037835	-1.948492209	0.015096312
ENSCAFG00000037891	1.136005698	0.000444791
ENSCAFG00000038320	-2.280863328	0.000535149
ENSCAFG00000038408	1.863437754	0.002241063
ENSCAFG00000038525	-1.380440645	6.19E-08
ENSCAFG00000038692	-1.277799042	0.01923605
ENSCAFG00000038722	3.048776788	0.038657025
ENSCAFG00000039280	1.030014058	0.036862642
ENSCAFG00000039524	5.979630986	0.040417525
ENSCAFG00000039836	2.327484717	0.019148216
ENSCAFG00000039851	1.897559504	0.025742449
ENSCAFG00000040231	-1.616911241	0.000127063
ENSCAFG00000040365	2.896989593	0.025237029
ENSCAFG00000040425	-1.055143908	0.00985659
ENSCAFG00000040440	-1.017597659	0.02575049
ENSCAFG00000040534	1.79037991	0.000318101
ENSCAFG00000040611	2.06534937	0.04227302

Table S4: List of genes (as ensemble ID) presenting a Rescued expression profile in the Biceps femoris or in the Vastus lateralis of the dogs showing therapeutic benefits.

Rescued Biceps	Rescued Vastus		Rescued Common	Gene name
ENSCAFG0000000097	ENSCAFG0000000097		ENSCAFG0000000097	ERBB3
ENSCAFG0000000110	ENSCAFG0000000124		ENSCAFG0000000124	TIMELESS
ENSCAFG0000000124	ENSCAFG0000000420		ENSCAFG0000000611	MEGF10
ENSCAFG0000000282	ENSCAFG0000000426		ENSCAFG00000001287	TCP11
ENSCAFG0000000288	ENSCAFG0000000479		ENSCAFG00000001556	KCNK17
ENSCAFG0000000372	ENSCAFG0000000493		ENSCAFG00000001596	FOXP4
ENSCAFG0000000413	ENSCAFG0000000522		ENSCAFG00000001649	GCNT1
ENSCAFG0000000448	ENSCAFG0000000535		ENSCAFG00000001793	BTBD11
ENSCAFG0000000523	ENSCAFG0000000568		ENSCAFG00000001909	KIF24
ENSCAFG0000000561	ENSCAFG0000000569		ENSCAFG00000002319	KIAA1211L
ENSCAFG0000000611	ENSCAFG0000000611		ENSCAFG00000002830	RIMS3
ENSCAFG0000000722	ENSCAFG0000000626		ENSCAFG00000003096	PM20D2
ENSCAFG0000000733	ENSCAFG0000000640		ENSCAFG00000003775	OSR1
ENSCAFG0000000799	ENSCAFG0000000641		ENSCAFG00000003804	
ENSCAFG0000000886	ENSCAFG0000000654		ENSCAFG00000003960	TRAF3IP2
ENSCAFG0000000903	ENSCAFG0000000671		ENSCAFG00000004127	SESN3
ENSCAFG0000000934	ENSCAFG0000000798		ENSCAFG00000004297	CCDC8
ENSCAFG00000001007	ENSCAFG0000000884		ENSCAFG00000004331	
ENSCAFG00000001067	ENSCAFG00000001126		ENSCAFG00000004481	SLC6A6
ENSCAFG00000001085	ENSCAFG00000001250		ENSCAFG00000004636	BCAM
ENSCAFG00000001287	ENSCAFG00000001287		ENSCAFG00000004731	TENM4
ENSCAFG00000001346	ENSCAFG00000001299		ENSCAFG00000004746	XRCC1
ENSCAFG00000001450	ENSCAFG00000001317		ENSCAFG00000004769	OPTN
ENSCAFG00000001556	ENSCAFG00000001324		ENSCAFG00000004820	ITGA9
ENSCAFG00000001581	ENSCAFG00000001453		ENSCAFG00000004958	ATP1A3
ENSCAFG00000001596	ENSCAFG00000001515		ENSCAFG00000005294	TK1
ENSCAFG00000001649	ENSCAFG00000001556		ENSCAFG00000005348	EHD3
ENSCAFG00000001793	ENSCAFG00000001596		ENSCAFG00000005433	ABCC4
ENSCAFG00000001875	ENSCAFG00000001649		ENSCAFG00000005564	UCP2
ENSCAFG00000001909	ENSCAFG00000001672		ENSCAFG00000006006	FASN
ENSCAFG00000001923	ENSCAFG00000001705		ENSCAFG00000006053	
ENSCAFG00000002313	ENSCAFG00000001793		ENSCAFG00000006800	FZD10
ENSCAFG00000002319	ENSCAFG00000001852		ENSCAFG00000006877	FAM110A
ENSCAFG00000002517	ENSCAFG00000001854		ENSCAFG00000007562	AMPD3
ENSCAFG00000002549	ENSCAFG00000001909		ENSCAFG00000007945	PROCR
ENSCAFG00000002656	ENSCAFG00000001966		ENSCAFG00000008062	
ENSCAFG00000002719	ENSCAFG00000002040		ENSCAFG00000008319	CHODL
ENSCAFG00000002748	ENSCAFG00000002042		ENSCAFG00000008707	CKMT2
ENSCAFG00000002796	ENSCAFG00000002053		ENSCAFG00000008786	NNAT
ENSCAFG00000002830	ENSCAFG00000002069		ENSCAFG00000008977	LRP4
ENSCAFG00000002854	ENSCAFG00000002079		ENSCAFG00000009066	MYOD1
ENSCAFG00000002917	ENSCAFG00000002098		ENSCAFG00000009333	CES1
ENSCAFG00000002928	ENSCAFG00000002116		ENSCAFG00000009337	TUBB2A
ENSCAFG00000003096	ENSCAFG00000002230		ENSCAFG00000009673	
ENSCAFG00000003276	ENSCAFG00000002319		ENSCAFG00000009777	NAV2
ENSCAFG00000003327	ENSCAFG00000002365		ENSCAFG00000009978	ETS2
ENSCAFG00000003388	ENSCAFG00000002420		ENSCAFG00000010090	IGF2

ENSCAFG00000003426	ENSCAFG00000002432	ENSCAFG000000010121	CD81
ENSCAFG00000003602	ENSCAFG00000002576	ENSCAFG000000010175	CDH22
ENSCAFG00000003663	ENSCAFG00000002645	ENSCAFG000000010288	MYBPH
ENSCAFG00000003676	ENSCAFG00000002830	ENSCAFG000000010309	MYOG
ENSCAFG00000003720	ENSCAFG00000002927	ENSCAFG000000010423	COL4A4
ENSCAFG00000003775	ENSCAFG00000002948	ENSCAFG000000010588	MARCKSL1
ENSCAFG00000003804	ENSCAFG00000002974	ENSCAFG000000010654	AGPAT3
ENSCAFG00000003824	ENSCAFG00000003096	ENSCAFG000000010936	NPNT
ENSCAFG00000003960	ENSCAFG00000003105	ENSCAFG000000011069	GJA5
ENSCAFG00000004034	ENSCAFG00000003116	ENSCAFG000000011283	CHRND
ENSCAFG00000004127	ENSCAFG00000003268	ENSCAFG000000011378	ANKRD34A
ENSCAFG00000004129	ENSCAFG00000003402	ENSCAFG000000011823	MN1
ENSCAFG00000004176	ENSCAFG00000003404	ENSCAFG000000012095	AHDC1
ENSCAFG00000004279	ENSCAFG00000003530	ENSCAFG000000012376	VASH2
ENSCAFG00000004297	ENSCAFG00000003579	ENSCAFG000000012525	MUC13
ENSCAFG00000004331	ENSCAFG00000003605	ENSCAFG000000012742	MTFP1
ENSCAFG00000004481	ENSCAFG00000003639	ENSCAFG000000012803	RIN1
ENSCAFG00000004510	ENSCAFG00000003775	ENSCAFG000000012824	SCN4B
ENSCAFG00000004529	ENSCAFG00000003797	ENSCAFG000000012904	CDK1
ENSCAFG00000004555	ENSCAFG00000003804	ENSCAFG000000012925	PHKA2
ENSCAFG00000004589	ENSCAFG00000003854	ENSCAFG000000013020	STMN3
ENSCAFG00000004636	ENSCAFG00000003960	ENSCAFG000000013283	CHRNA1
ENSCAFG00000004731	ENSCAFG00000004054	ENSCAFG000000013423	FUOM
ENSCAFG00000004746	ENSCAFG00000004124	ENSCAFG000000013483	TMEM120A
ENSCAFG00000004769	ENSCAFG00000004127	ENSCAFG000000013521	POLA1
ENSCAFG00000004820	ENSCAFG00000004137	ENSCAFG000000014054	ACHE
ENSCAFG00000004856	ENSCAFG00000004232	ENSCAFG000000014124	CHCHD10
ENSCAFG00000004931	ENSCAFG00000004274	ENSCAFG000000014308	ALAS2
ENSCAFG00000004958	ENSCAFG00000004297	ENSCAFG000000014310	APEX2
ENSCAFG00000005081	ENSCAFG00000004331	ENSCAFG000000014410	CHST3
ENSCAFG00000005122	ENSCAFG00000004392	ENSCAFG000000014448	ZNF804A
ENSCAFG00000005179	ENSCAFG00000004402	ENSCAFG000000014474	IGFBP5
ENSCAFG00000005276	ENSCAFG00000004416	ENSCAFG000000014551	GAL3ST4
ENSCAFG00000005294	ENSCAFG00000004481	ENSCAFG000000014978	
ENSCAFG00000005301	ENSCAFG00000004632	ENSCAFG000000015078	FAM184B
ENSCAFG00000005309	ENSCAFG00000004636	ENSCAFG000000015209	TUBA4A
ENSCAFG00000005348	ENSCAFG00000004714	ENSCAFG000000015217	
ENSCAFG00000005433	ENSCAFG00000004731	ENSCAFG000000015539	PAX7
ENSCAFG00000005468	ENSCAFG00000004746	ENSCAFG000000015788	B4GALNT3
ENSCAFG00000005564	ENSCAFG00000004769	ENSCAFG000000016072	
ENSCAFG00000005595	ENSCAFG00000004801	ENSCAFG000000016769	NES
ENSCAFG00000005621	ENSCAFG00000004820	ENSCAFG000000017615	ST8SIA5
ENSCAFG00000005768	ENSCAFG00000004956	ENSCAFG000000017705	ARMCX2
ENSCAFG00000005843	ENSCAFG00000004958	ENSCAFG000000017883	NRK
ENSCAFG00000005918	ENSCAFG00000004991	ENSCAFG000000018175	CAPN6
ENSCAFG00000005965	ENSCAFG00000005051	ENSCAFG000000018277	
ENSCAFG00000006006	ENSCAFG00000005183	ENSCAFG000000018360	
ENSCAFG00000006019	ENSCAFG00000005255	ENSCAFG000000018457	NT5M
ENSCAFG00000006053	ENSCAFG00000005294	ENSCAFG000000018643	SLC25A23
ENSCAFG00000006073	ENSCAFG00000005348	ENSCAFG000000018702	EFCAB7

ENSCAFG00000006134	ENSCAFG00000005365	ENSCAFG00000018864	GPC3
ENSCAFG00000006164	ENSCAFG00000005411	ENSCAFG00000019014	SEMA6B
ENSCAFG00000006175	ENSCAFG00000005433	ENSCAFG00000019230	ATP2B3
ENSCAFG00000006234	ENSCAFG00000005564	ENSCAFG00000019489	TP73
ENSCAFG00000006373	ENSCAFG00000005693	ENSCAFG00000019601	SOX8
ENSCAFG00000006381	ENSCAFG00000005723	ENSCAFG00000020153	MTSS1L
ENSCAFG00000006424	ENSCAFG00000005767	ENSCAFG00000020166	ANGPTL2
ENSCAFG00000006474	ENSCAFG00000005846	ENSCAFG00000020345	PTGFR
ENSCAFG00000006513	ENSCAFG00000005853	ENSCAFG00000020713	RF00279
ENSCAFG00000006576	ENSCAFG00000005960	ENSCAFG00000022843	MIR675
ENSCAFG00000006596	ENSCAFG00000005963	ENSCAFG00000023904	CHRNB4
ENSCAFG00000006723	ENSCAFG00000006006	ENSCAFG00000024609	CNTN2
ENSCAFG00000006800	ENSCAFG00000006022	ENSCAFG00000025390	SLC22A17
ENSCAFG00000006877	ENSCAFG00000006053	ENSCAFG00000028459	MT3
ENSCAFG00000007001	ENSCAFG00000006091	ENSCAFG00000028490	
ENSCAFG00000007047	ENSCAFG00000006100	ENSCAFG00000028594	RF01973
ENSCAFG00000007079	ENSCAFG00000006215	ENSCAFG00000028647	BGLAP
ENSCAFG00000007111	ENSCAFG00000006250	ENSCAFG00000028653	
ENSCAFG00000007149	ENSCAFG00000006264	ENSCAFG00000028761	
ENSCAFG00000007338	ENSCAFG00000006334	ENSCAFG00000028817	CFD
ENSCAFG00000007562	ENSCAFG00000006392	ENSCAFG00000028947	ELN
ENSCAFG00000007635	ENSCAFG00000006417	ENSCAFG00000028958	TCEAL7
ENSCAFG00000007847	ENSCAFG00000006528	ENSCAFG00000029004	
ENSCAFG00000007893	ENSCAFG00000006559	ENSCAFG00000029304	RF01972
ENSCAFG00000007936	ENSCAFG00000006563	ENSCAFG00000029856	RF01881
ENSCAFG00000007945	ENSCAFG00000006608	ENSCAFG00000030198	
ENSCAFG00000007985	ENSCAFG00000006612	ENSCAFG00000031239	
ENSCAFG00000008062	ENSCAFG00000006701	ENSCAFG00000031481	
ENSCAFG00000008123	ENSCAFG00000006740	ENSCAFG00000031936	NRBF2
ENSCAFG00000008295	ENSCAFG00000006745	ENSCAFG00000032024	GPR162
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ENSCAFG00000008582	ENSCAFG00000006909	ENSCAFG00000032235	
ENSCAFG00000008707	ENSCAFG00000006930	ENSCAFG00000032286	
ENSCAFG00000008755	ENSCAFG00000007036	ENSCAFG00000032403	MAP3K7CL
ENSCAFG00000008786	ENSCAFG00000007045	ENSCAFG00000032684	
ENSCAFG00000008795	ENSCAFG00000007082	ENSCAFG00000032896	
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ENSCAFG00000008977	ENSCAFG00000007407	ENSCAFG00000033312	
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ENSCAFG00000009097	ENSCAFG00000007626	ENSCAFG00000038320	
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ENSCAFG00000009105	ENSCAFG00000007653		
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ENSCAFG00000009187	ENSCAFG00000007845		
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ENSCAFG00000009333	ENSCAFG00000007945		

ENSCAFG00000009337	ENSCAFG00000008062
ENSCAFG00000009441	ENSCAFG00000008164
ENSCAFG00000009506	ENSCAFG00000008319
ENSCAFG00000009596	ENSCAFG00000008343
ENSCAFG00000009649	ENSCAFG00000008403
ENSCAFG00000009664	ENSCAFG00000008477
ENSCAFG00000009673	ENSCAFG00000008503
ENSCAFG00000009721	ENSCAFG00000008566
ENSCAFG00000009777	ENSCAFG00000008597
ENSCAFG00000009869	ENSCAFG00000008707
ENSCAFG00000009951	ENSCAFG00000008728
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ENSCAFG00000017883	NRK	4.56944269	2.99E-09	5.018412332	3.84E-05
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ENSCAFG00000008977	LRP4	2.637229703	4.82E-08	1.641310401	0.005441352
ENSCAFG00000014978	PIK3R2	2.333590538	1.59E-07	1.513989504	0.000142868
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ENSCAFG00000018702	EFCAB7	-2.524855109	9.40E-07	-2.44506268	0.000325149
ENSCAFG00000012803	RIN1	3.155806278	1.42E-06	3.401147284	4.51E-07
ENSCAFG00000012095	AHDC1	1.437749831	1.51E-06	1.115106058	6.09E-05
ENSCAFG0000001596	FOXP4	2.091095449	3.82E-06	1.408734717	0.002101039
ENSCAFG00000010121	CD81	1.393565596	4.59E-06	1.451217502	7.66E-05
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ENSCAFG00000020153	MTSS1L	1.737018296	5.57E-06	1.5078105	0.000541826
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ENSCAFG00000002830	RIMS3	-3.512294484	1.20E-05	-3.999533931	1.15E-05
ENSCAFG00000010090	IGF2	3.240827274	1.30E-05	3.259644778	6.39E-07
ENSCAFG00000015217	NA	-2.109544247	1.43E-05	-1.689554354	0.013928389
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ENSCAFG00000009337	TUBB2A	3.250224395	1.47E-05	3.341008052	1.38E-06
ENSCAFG00000013423	FUOM	-2.263366815	1.50E-05	-1.046372489	0.044613704
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ENSCAFG00000015209	TUBA4A	-2.085553592	2.82E-05	-1.515768766	0.021585318
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ENSCAFG00000013283	CHRNA1	3.815468255	3.47E-05	2.96060933	6.85E-06
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ENSCAFG00000032024	GPR162	-2.463949496	6.21E-05	-2.026932174	0.018745273
ENSCAFG0000001556	KCNK17	2.305177845	7.20E-05	1.911230967	0.003774034
ENSCAFG00000013483	TMEM120A	-1.405061093	7.87E-05	-1.025962526	0.045893036
ENSCAFG00000004127	SESN3	2.678404538	7.91E-05	2.238837004	0.000578787
ENSCAFG00000014448	ZNF804A	3.324081824	8.51E-05	2.829881295	0.000117067
ENSCAFG00000005564	UCP2	1.582672682	9.22E-05	1.729419299	4.62E-05
ENSCAFG00000017705	ARMCX2	2.602599203	9.83E-05	2.429860868	5.15E-05
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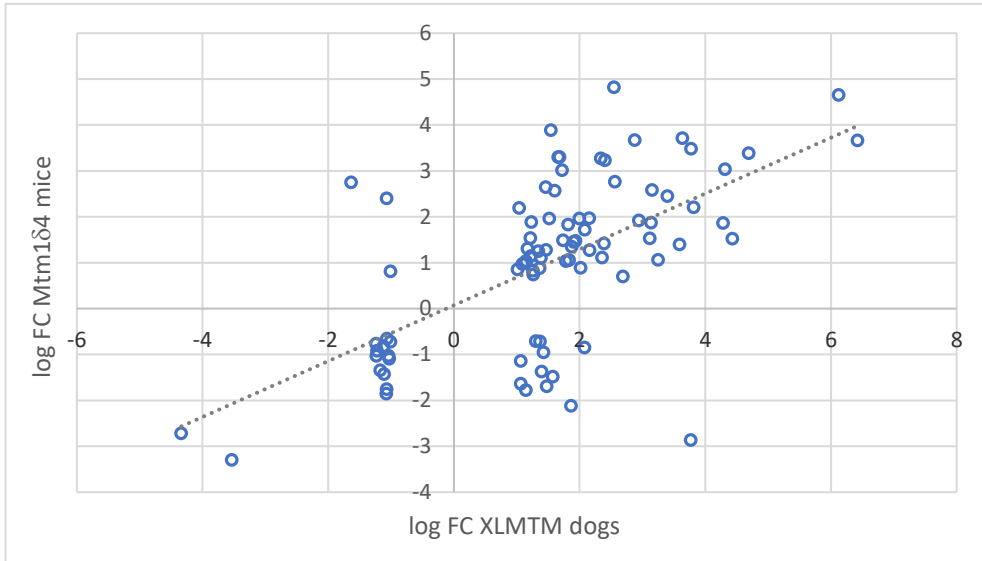
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ENSCAFG00000001909	KIF24	1.81716916	0.001685762	1.588874132	0.019182574
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ENSCAFG00000024609	CNTN2	2.872419854	0.001725726	2.173429773	0.001163142
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ENSCAFG00000029004	NA	-1.599186648	0.002268363	-1.282023553	0.000261259
ENSCAFG00000004731	TENM4	1.9804845	0.002295963	1.215926441	0.015058305
ENSCAFG00000016769	NES	1.905412123	0.002378304	1.588578298	0.000185377
ENSCAFG00000004820	ITGA9	1.722472476	0.00240463	1.745010553	0.011866798
ENSCAFG00000010654	AGPAT3	-1.181973406	0.002425076	-1.539330593	0.000540829
ENSCAFG00000004481	SLC6A6	1.975231116	0.002518781	1.469677251	0.01518367
ENSCAFG00000012824	SCN4B	-1.59412924	0.002692617	-1.504353536	0.011297857
ENSCAFG00000006006	FASN	1.832543195	0.002831356	1.294402294	0.001018038
ENSCAFG00000028653	NA	3.005018503	0.002895369	1.907294955	0.005967732
ENSCAFG00000000097	ERBB3	2.836526719	0.003004938	1.998549435	0.033243834
ENSCAFG00000018277	CKB	2.255816402	0.003192217	2.127094967	0.002477956
ENSCAFG00000025390	SLC22A17	2.258264891	0.003516952	2.037490459	7.29E-05
ENSCAFG00000012376	VASH2	2.084699386	0.003572492	2.13234889	0.002908275
ENSCAFG00000018643	SLC25A23	1.637985631	0.003785276	2.196647327	0.001546382
ENSCAFG00000004636	BCAM	1.431501768	0.004542265	1.295091518	0.003081894
ENSCAFG00000010936	NPNT	2.260581185	0.005488884	3.560697738	2.55E-06
ENSCAFG00000017615	ST8SIA5	-1.236747114	0.005677044	-1.110632021	0.005813318
ENSCAFG00000014054	ACHE	2.39967239	0.005847406	1.710129314	0.048663979
ENSCAFG00000022843	NA	2.622702983	0.006007069	3.958896054	3.01E-05
ENSCAFG00000019230	ATP2B3	1.951482529	0.006389196	1.70976847	0.048857846
ENSCAFG00000012525	MUC13	3.62251399	0.006464476	4.227125415	3.81E-05
ENSCAFG00000001793	BTBD11	1.551643808	0.00653172	1.598625367	0.000403856
ENSCAFG00000005433	ABCC4	-1.235849924	0.006665142	-1.052007752	0.023438786
ENSCAFG00000029304	NA	2.581346343	0.006723539	4.270157482	7.95E-06
ENSCAFG00000028490	NA	2.134516548	0.008739537	1.789188253	0.032227547
ENSCAFG00000010309	MYOG	1.52088885	0.009245696	1.845085992	0.000214655
ENSCAFG00000028594	NA	2.538790086	0.009764673	3.791728862	3.18E-05
ENSCAFG00000020345	PTGFR	-1.882157801	0.009963985	-2.753228159	0.00230441
ENSCAFG00000007562	AMPD3	1.849416153	0.01014497	2.671833403	0.002075467
ENSCAFG00000014124	CHCHD10	-1.597283739	0.010210759	-1.340562915	0.001679647
ENSCAFG00000035199	NA	2.07300263	0.010484605	3.601068114	0.000318009
ENSCAFG00000016072	NA	1.103191687	0.011734775	1.667366588	0.014967357
ENSCAFG00000004769	OPTN	-1.512936657	0.011889457	-1.375357781	2.56E-05
ENSCAFG00000012742	MTFP1	-1.929641457	0.012633578	-1.538109123	0.002995437
ENSCAFG00000014410	CHST3	1.156284932	0.012681418	1.108767486	0.029641832
ENSCAFG00000000124	TIMELESS	1.393514773	0.013025503	1.664271664	0.000601602
ENSCAFG00000014551	GAL3ST4	1.729897576	0.013455288	1.78265139	0.023465333
ENSCAFG00000008707	CKMT2	-1.513175637	0.014869607	-1.217424522	0.002846116
ENSCAFG00000033011	NA	-2.743409349	0.015945439	-2.74985822	0.019972755
ENSCAFG00000008786	NNAT	1.385895771	0.017606039	1.860409249	0.000386359
ENSCAFG00000004958	ATP1A3	-1.916108938	0.019185539	-2.120277144	0.002303361
ENSCAFG00000035036	NA	-1.682876794	0.019500818	-1.834187032	0.024883428

ENSCAFG00000010175	CDH22	-1.376839677	0.019541391	-2.459550185	0.001622257
ENSCAFG00000005294	TK1	1.370300308	0.020792332	1.779067613	1.88E-05
ENSCAFG00000029856	NA	10.4738747	0.020926299	8.020069827	0.020049372
ENSCAFG00000032235	NA	1.063675433	0.022272439	1.144905011	0.008093552
ENSCAFG00000010588	MARCKSL1	1.800448811	0.022793028	2.770710906	0.002324573
ENSCAFG00000005348	EHD3	1.844069921	0.025868063	1.994919366	0.010967516
ENSCAFG00000011378	ANKRD34A	1.637426544	0.027794058	2.50229108	0.016144896
ENSCAFG00000009066	MYOD1	1.704728854	0.029840809	1.279295476	0.017776792
ENSCAFG00000012925	PHKA2	1.382655474	0.032619048	1.307547992	0.04544663

Table S6: Correlation analysis between the expression changes observed in XLMTM dogs and Mtm1 KO mice for the 87 differentially expressed genes detected in both species.

ensembl ID	Gene name	log FC dogs	log FC mice
ENSCAFG00000011513	ABLIM1	1.73670291	1.489
ENSCAFG00000012181	ACTC1	3.772649425	-2.867
ENSCAFG00000016453	ADGRL1	1.307586207	-0.711
ENSCAFG00000012013	ANPEP	1.834642459	1.053
ENSCAFG00000016550	ASB12	-1.234678707	-0.766
ENSCAFG00000010942	CCDC91	-1.22278308	-0.919
ENSCAFG00000029853	CDKN1A	2.880122608	3.665
ENSCAFG00000013283	CHRNA1	3.815468255	2.206
ENSCAFG00000011283	CHRND	4.316764066	3.037
ENSCAFG00000024807	CHRNA1	6.422497873	3.662
ENSCAFG00000017138	CILP	2.340963786	3.274
ENSCAFG00000006035	COL6A6	1.373634224	-0.721
ENSCAFG00000008761	CX3CL1	-1.631523824	2.749
ENSCAFG00000006231	DCLK1	3.592784876	1.394
ENSCAFG00000009653	DOP1B	2.080276665	-0.853
ENSCAFG00000002919	EFEMP1	1.429460589	-0.953
ENSCAFG00000011772	EGLN1	-1.064307644	-0.655
ENSCAFG00000009869	EHD4	1.260345827	0.824
ENSCAFG00000018959	EMP2	1.219309968	1.535
ENSCAFG00000014323	EPHB2	2.391796378	1.419
ENSCAFG00000028669	FAM171B	1.876683757	1.347
ENSCAFG00000015272	FGFBP1	-3.536343867	-3.299
ENSCAFG00000016518	FGFR4	1.145955705	-1.779
ENSCAFG00000002105	FHL2	1.817158446	1.826
ENSCAFG00000006019	FREM2	1.997135963	1.959
ENSCAFG00000018405	FST	4.433409456	1.519
ENSCAFG00000006421	GAS6	-1.009584253	0.808
ENSCAFG00000012428	HES6	1.36513027	0.876
ENSCAFG00000002576	HIVEP3	2.159868089	1.269
ENSCAFG00000009074	HOMER1	-1.107945461	-1.426
ENSCAFG00000001336	ISCA1	-1.007809986	-0.728
ENSCAFG00000005037	KLF5	1.236429367	1.881
ENSCAFG00000006840	LDLRAD3	1.386681603	1.101
ENSCAFG00000005960	LRRN1	1.468728589	1.274
ENSCAFG00000016465	MAGED2	1.263446026	0.739
ENSCAFG00000010758	MAP2K6	1.574037058	-1.483
ENSCAFG00000005963	METTL21C	-4.337630234	-2.716
ENSCAFG00000009110	MT1E	1.684552853	3.302
ENSCAFG00000023759	MT2A	2.547857727	4.818
ENSCAFG00000028459	MT3	6.12600805	4.655
ENSCAFG00000013728	MYL4	3.638724975	3.71
ENSCAFG00000010309	MYOG	1.52088885	1.958
ENSCAFG00000009777	NAV2	2.360013976	1.107
ENSCAFG00000013844	NCAM1	3.120117838	1.531
ENSCAFG00000016769	NES	1.905412123	1.45
ENSCAFG00000003720	NRCAM	4.283879136	1.864

ENSCAFG00000032227	OLFM1	2.018599342	0.883
ENSCAFG00000015539	PAX7	1.395532008	-1.376
ENSCAFG00000010225	PHKB	-1.025976526	-1.095
ENSCAFG00000009076	PLBD2	2.689637486	0.7
ENSCAFG00000005362	PLD3	1.089200362	0.973
ENSCAFG00000003096	PM20D2	1.866701978	-2.123
ENSCAFG00000018654	PRR32	2.403978145	3.226
ENSCAFG00000001646	PRUNE2	3.399318155	2.448
ENSCAFG00000005870	RASGRP3	-1.037928066	-1.032
ENSCAFG00000006528	RASSF7	1.720814154	3.01
ENSCAFG00000012803	RIN1	3.155806278	2.583
ENSCAFG00000009596	RUNX1	2.563379593	2.759
ENSCAFG00000005839	SATB1	-1.232135107	-1.032
ENSCAFG00000012082	SEMA4B	1.228537847	1.143
ENSCAFG00000012290	SFN	1.462504245	2.642
ENSCAFG00000019194	SLC43A2	1.785886391	1.035
ENSCAFG00000008028	SLC9A9	1.345211158	1.247
ENSCAFG00000012460	SMYD2	-1.16803138	-1.346
ENSCAFG00000004374	SOX9	2.155439117	1.965
ENSCAFG00000004500	SYTL2	-1.06740374	-1.759
ENSCAFG000000032112	TAL2	2.94392871	1.918
ENSCAFG00000011533	TARBP1	1.065472211	-1.641
ENSCAFG00000012517	TMOD4	-1.118371009	-0.822
ENSCAFG00000010798	TNNT2	3.137959501	1.868
ENSCAFG00000014443	TSC22D4	1.17473527	1.301
ENSCAFG00000009337	TUBB2A	3.250224395	1.063
ENSCAFG00000018832	TUBB6	1.60572272	2.568
ENSCAFG00000015878	UCHL1	1.546077843	3.884
ENSCAFG00000013489	UCK2	1.936783208	1.469
ENSCAFG00000012376	VASH2	2.084699386	1.714
ENSCAFG00000013039	ZNF365	-1.070865273	2.396
ENSCAFG00000015731	ZNF385C	4.692270181	3.38
ENSCAFG00000001985	ENSMUSG000	1.039690188	2.188
ENSCAFG00000003564	ENSMUSG000	1.015664287	0.849
ENSCAFG00000003676	ENSMUSG000	-1.074228768	-1.857
ENSCAFG00000004124	ENSMUSG000	1.144810094	1.034
ENSCAFG00000009113	ENSMUSG000	1.662637003	3.302
ENSCAFG00000011368	ENSMUSG000	1.480762529	-1.692
ENSCAFG00000023152	ENSMUSG000	1.153009884	1.008
ENSCAFG00000030662	ENSMUSG000	3.778100823	3.483
ENSCAFG00000032235	ENSMUSG000	1.063675433	-1.146



Spearman rank correlation $r = 0.6$
p-value $1.1E-9$

Supplemental Methods:

Detailed below is the raw R code used to analyse the RNA-sequencing count tables

```
# Import .csv files: read counts (count_table.csv), information about
samples and groups (samples_info.csv), and gene annotation file
(gene_info.csv)
> samples_info <- read_csv("samples_info.csv")
> count_table <- read_csv("count_table.csv")
> gene_info <- read_csv("gene_info.csv")

# Call the packages necessary for data processing and analysis
> library(limma)
> library(edgeR)
> library(genefilter)
> library(pheatmap)
> library(viridis)
> library(dplyr)

# Reformat count_table into a matrix of counts with row.names corresponding
to the column of gene_info which will be used for gene annotation (e.g.
ensembl identifiers). Requires same number of lines in count_table.csv and
gene_info.csv
> Mat<-as.matrix(count_table[,2:14])
> row.names(Mat)<-count_table$Gene_id

# Create a DGEList object, filtering off the genes not expressed in any dog
> DGE<-DGEList(counts=Mat, lib.size=colSums(Mat),
norm.factors=rep(1,ncol(Mat)), samples=samples_info, genes=gene_info,
remove.zeros=TRUE)
Removing x rows with all zero counts

# Transform raw counts into count per million reads (cpm), and log(cpm)
> DGEcpm<-cpm(DGE, log=FALSE)
> DGElcpm<-cpm(DGE, log=TRUE)

# keep only genes with cpm>1 in at least 3 Dogs
> keep.exprs<-rowSums(DGEcpm>1)>=3
> DGE<-DGE[keep.exprs, , keep.lib.sizes=FALSE]
> DGElcpm<-cpm(DGE, log=TRUE)

# incorporate normalization (scaling) factors to reduce heteroscedasticity,
using the trimmed mean of M-values (TMM) method
> DGE<-calcNormFactors(DGE, method="TMM")

# Genewise Negative Binomial Generalized Linear Fitting using the edgeR
package
> design<-model.matrix(~0+Treatment)
> colnames(design)<-gsub("Treatment", "", colnames(design))
# 'Treatment' corresponds to the name of the column in the
"samples_info.csv" file on which the statistical comparison is performed.
> estdisp<-estimateDisp(BicepsDGE, design)
> fit<-glmFit(estdisp, design)

# Factors=c("AAVHigh", "AAVLow", "AAVMid", "WT", "None")
> lrt<-glmLRT(fit, contrast=c(0,0,0,-1,1)) # hence contrast=None-WT

# Subset DE genes: p value ≤ 0.05 & fold change ≥ 2 or ≤ -2
> DE_genes<-lrt[which(lrt$table$PValue<=0.05 & abs(lrt$table$logFC)>1),]

# Same analysis done for contrast=c(1,0,0,0,-1), named lrt2 and DE_genes2
```

```

and c(1,0,0,-1,0), named lrt3 and DE_genes3

# Extract list of Rescued genes in AAVHigh dogs = common genes between
DE_genes and DE_genes2 that are not present in DE_genes3
> RescHigh<-dplyr::semi_join(DE_genes$genes, DE_genes2$genes, by="X1")
> RescHigh<-dplyr::anti_join(RescHigh, DE_genes3$genes, by="X1")

# Extract list of Resistant genes in AAVHigh dogs = common genes between
DE_genes1 and DE_genes3 that are not present in DE_genes2
> ResistHigh<-dplyr::semi_join(DE_genes$genes, DE_genes3$genes, by="X1")
> ResistHigh<-dplyr::anti_join(ResistHigh, DE_genes2$genes, by="X1")

# Extract list of Induced genes in AAVHigh dogs = common genes between
DE_genes2 and DE_genes3 that are not present in DE_genes
> IndHigh<-dplyr::semi_join(DE_genes2true$genes, DE_genes3$genes, by="X1")
> IndHigh<-dplyr::anti_join(IndHigh, DE_genes$genes, by="X1")

# Extract list of DE genes that are present in DE_genes, DE_genes2, and
DE_genes3.
> TriHigh<-dplyr::intersect(DE_genes$genes, DE_genes2$genes)
> TriHigh<-dplyr::intersect(TriHigh, DE_genes3$genes)
> length(TriHigh$X1)

# Create a matrix with grouped median lcpm values of TriHigh genes
> TriHighMat<-matrix(c(1:12),nrow=4,ncol=3)
> row.names(TriHighMat)<-TriHigh$X1
> colnames(TriHighMat)<-c("WT","XLMTM","AAVHigh")
> for(i in 1:4){
+   TriHighMat[i,1]<-(DGEIcpm[TriHigh[i,1],1]+DGEIcpm[TriHigh[i,1],7])/2
+   TriHighMat[i,2]<-
(DGEIcpm[TriHigh[i,1],4]+DGEIcpm[TriHigh[i,1],8]+DGEIcpm[TriHigh[i,1],10])/
3
+   TriHighMat[i,3]<-
(DGEIcpm[TriHigh[i,1],12]+DGEIcpm[TriHigh[i,1],13])/2
+   }

# Use operators to extract lists of Partially Rescued and Worsened genes
> PartHigh<-which((TriHighMat[,1]<TriHighMat[,3] &
TriHighMat[,3]<TriHighMat[,2]) | (TriHighMat[,1]>TriHighMat[,3] &
TriHighMat[,3]>TriHighMat[,2]))
> WorHigh<-which((TriHighMat[,1]<TriHighMat[,2] &
TriHighMat[,2]<TriHighMat[,3]) | (TriHighMat[,1]>TriHighMat[,2] &
TriHighMat[,2]>TriHighMat[,3]))

# Similar analyses can be performed for AAVMid and AAVLow dogs by changing
the contrasts taken as inputs for lrt2 and lrt3

```