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Supplemental Information

Multi-omics comparisons of different forms of centronuclear myopathies and the effects of several therapeutic strategies

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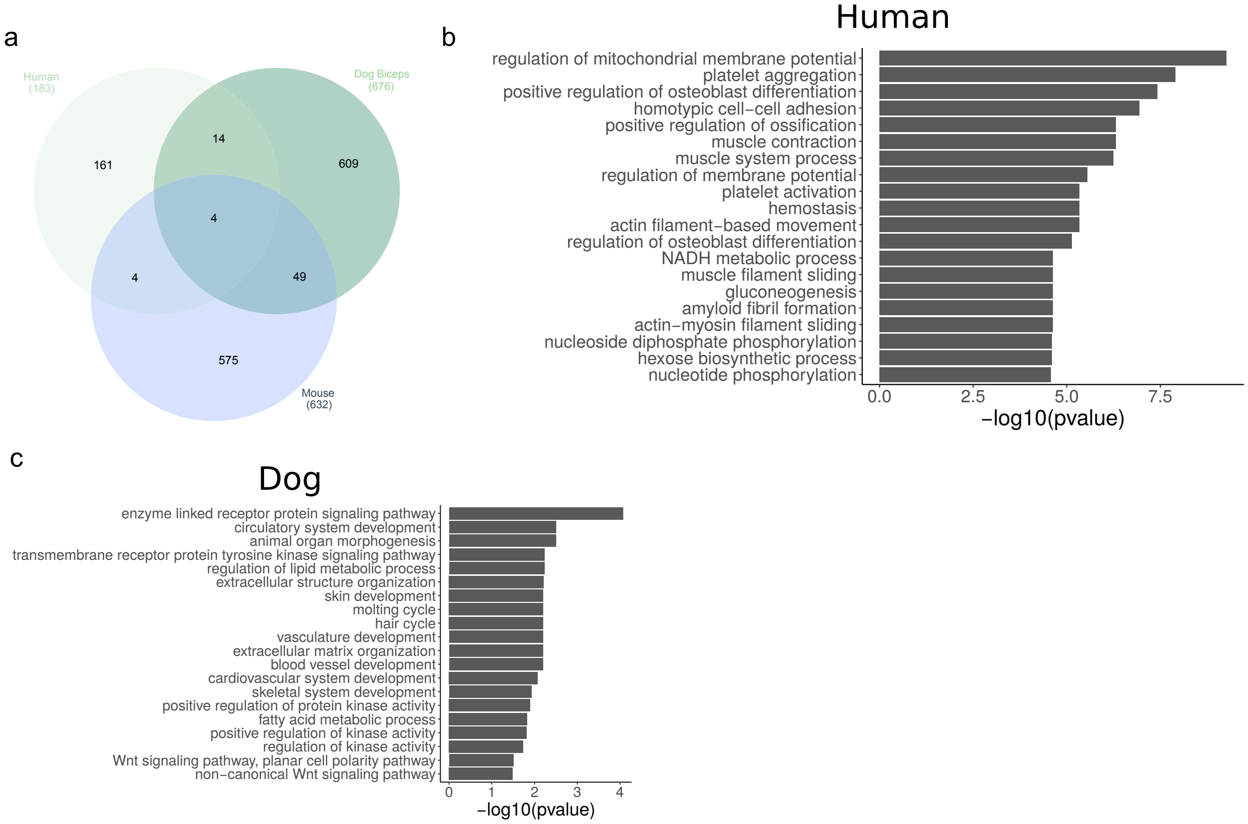

Figure S1. (a)Venn diagram illustrating the common dysregulated genes based on the MTM1 vs controls comparison in three different species: human, mice and dog (Biceps femoris). (b-c) Gene Ontology (GO) enrichment analysis of the specific differentially expressed genes in (b) Human cohort and (c) in Dog cohort. The 20 GO biological process terms with the lowest p-value are displayed.

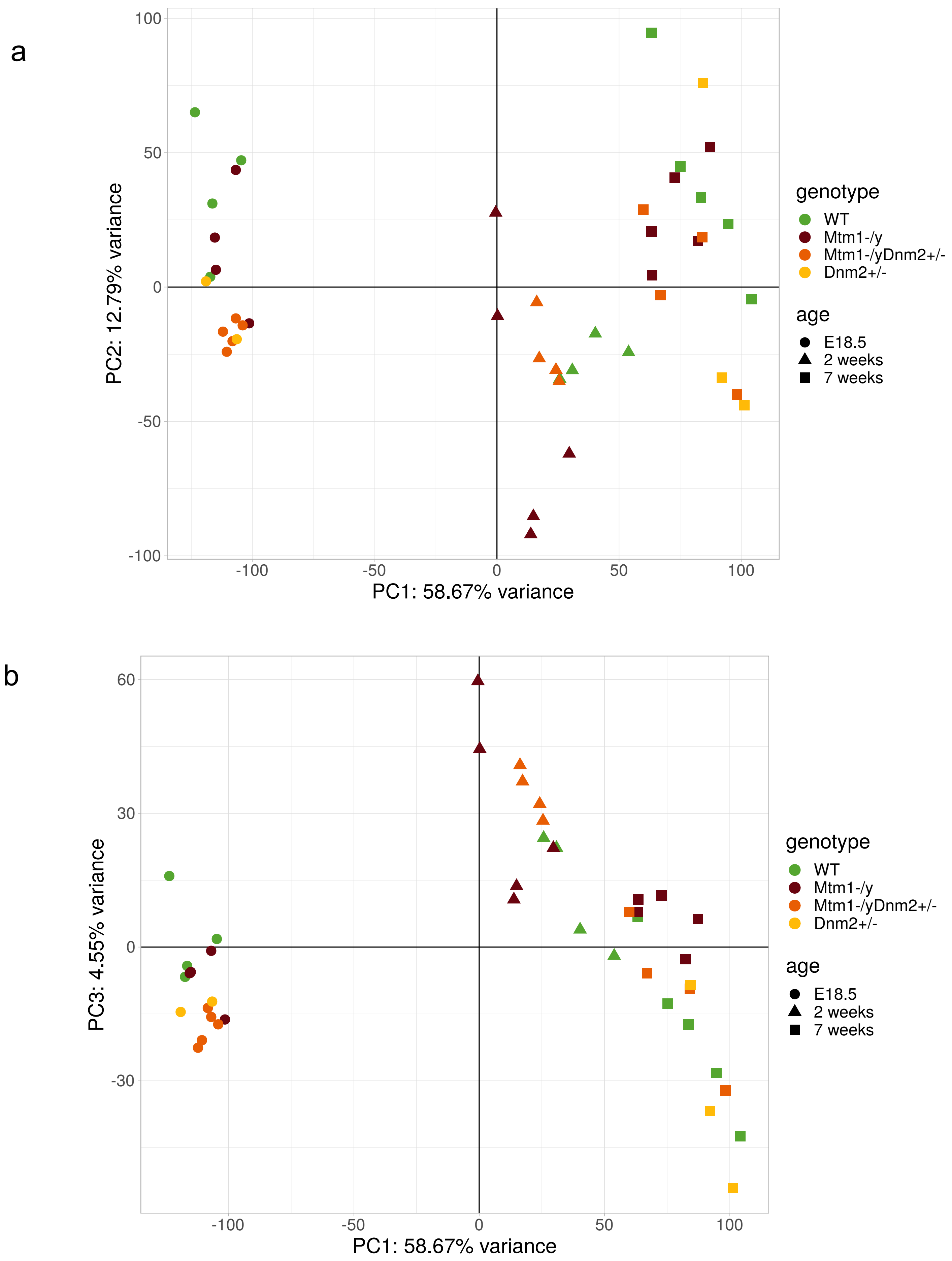

Figure S2. PCA related to Fig 5b. (a) PC1 and PC2 and (b) PC1 and PC3 are represented.

Figure S3. GO enrichment analysis for biological processes (BP), cellular component (CC) and molecular function (MF) of the differentially expressed genes in Mtm1-/y vs WT mice (N =1175 genes) at (a) 2 w and (b) at 7 w (N=1981 genes). GO terms with highest ratio and lowest q-value are represented. The ratio represents the number of genes dysregulated divided by the total number of genes in the category. The color scale is based on the q-value, dark colors indicate most significantly over-represented terms, while lighter colors indicate the least significant terms.

Figure S4. mRNA expression levels of genes of interest in diseased, rescued and control mice in the MTM1-a cohort at 2 w. Boxplots displaying normalized Ct values. Pairwise significance calculated by Dunn's test, $p < 0.05$ are represented in bold.

Figure S5. mRNA expression levels of genes of interest in diseased, rescued and control mice in the MTM1-a cohort at 7 w. Boxplots displaying normalized Ct values. Pairwise significance calculated by Dunn's test, $p < 0.05$ are represented in bold.

Figure S6. GO enrichment analysis for biological processes (BP), cellular component (CC) and molecular function (MF) of the differentially expressed proteins in Mtm1-/y vs WT mice (N =168 proteins) at (a) 2w and (b) at 7 w (N=496 proteins). GO terms with highest ratio and lowest q-value are represented. The ratio represents the number of proteins dysregulated divided by the total number of proteins in the category. The color scale is based on the q-value, dark colors indicate most significantly over-represented terms, while lighter colors indicate the least significant terms.

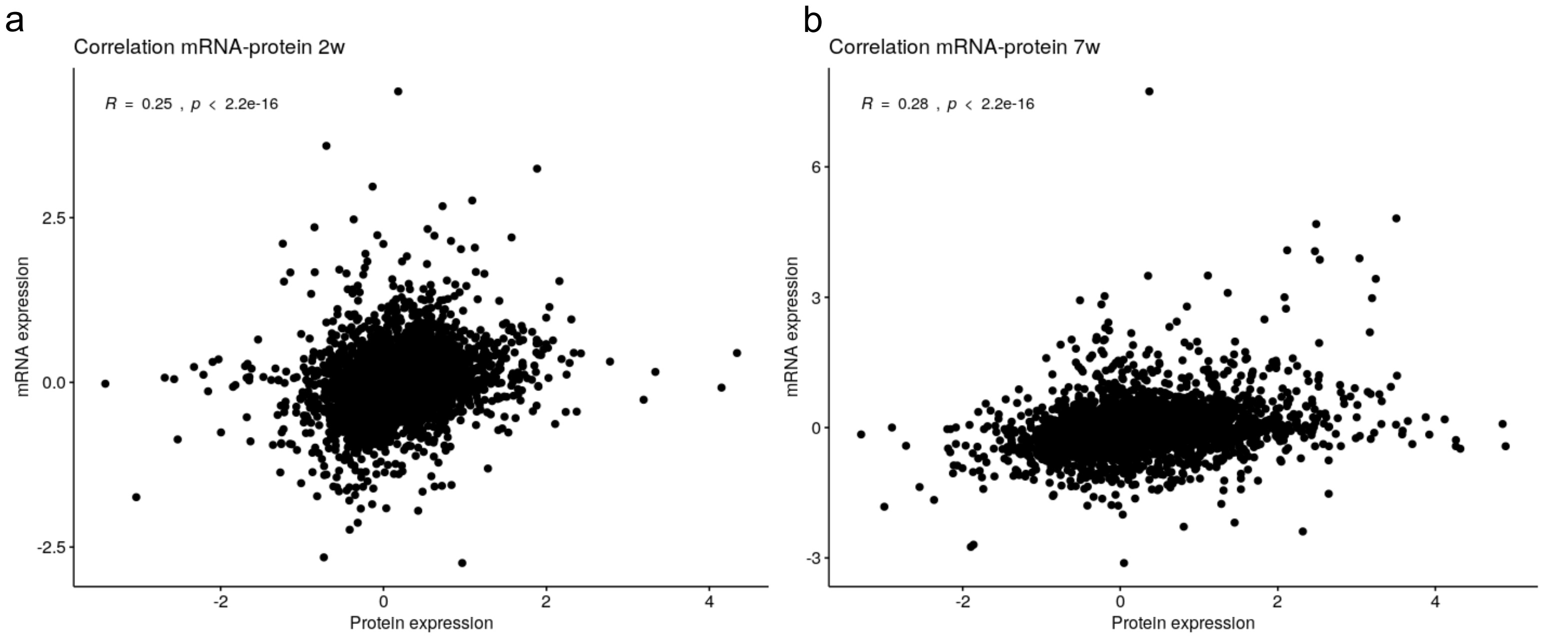

Figure S7. Pearson correlation between mRNA and protein levels measured by RNASeq and mass spectrometry (a) at 2 w and (b) at 7 w.

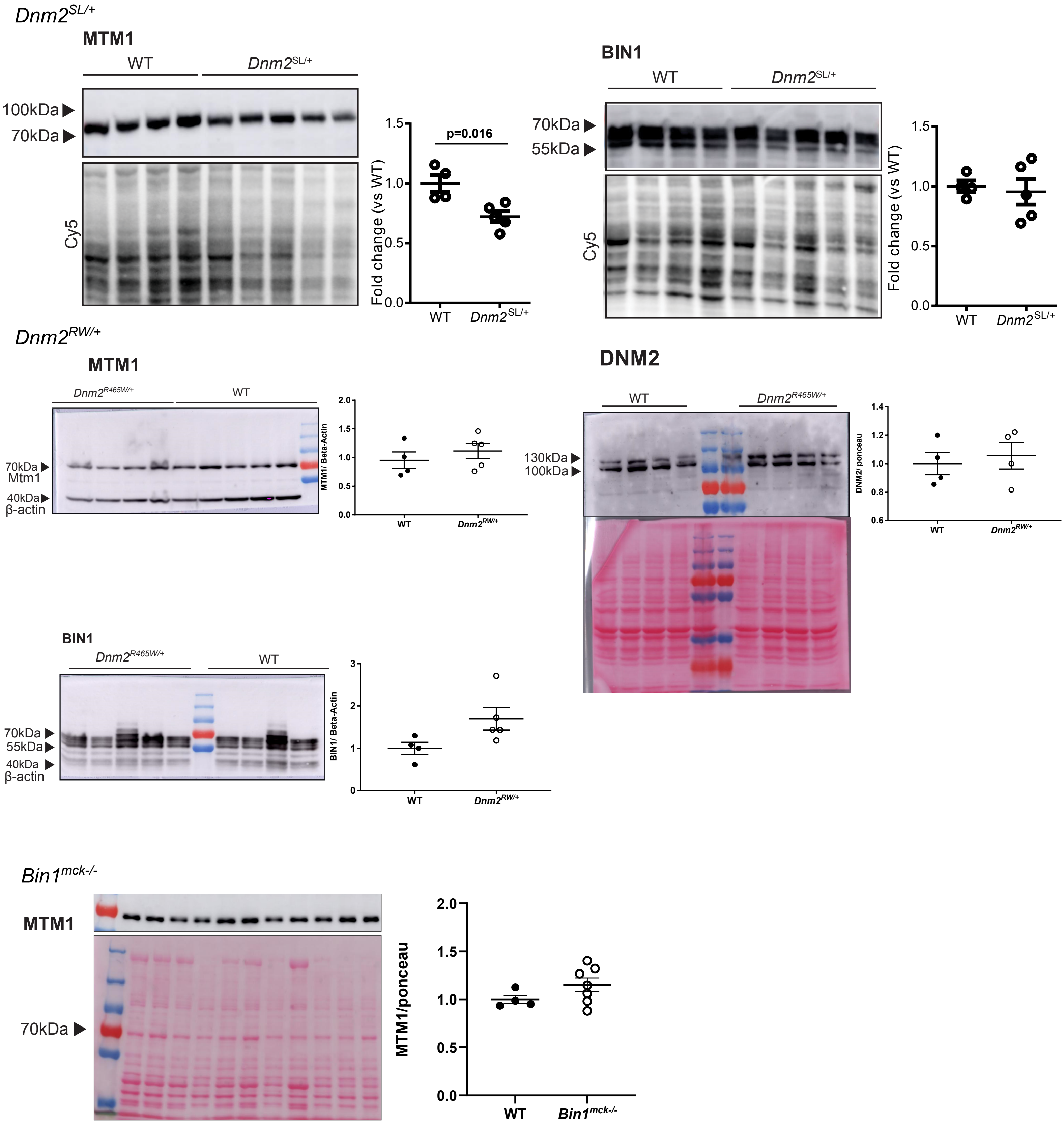

Figure S8. MTM1 and BIN1 protein levels in Dnm2SL/+ Tibialis anterior muscles. MTM1, BIN1 and DNM2 protein levels in Dnm2RW/+ TA muscles. MTM1 protein level in Bin1mck-/- TA muscles. Pairwise significance calculated by t-test, $p < 0.05$ are represented in bold.

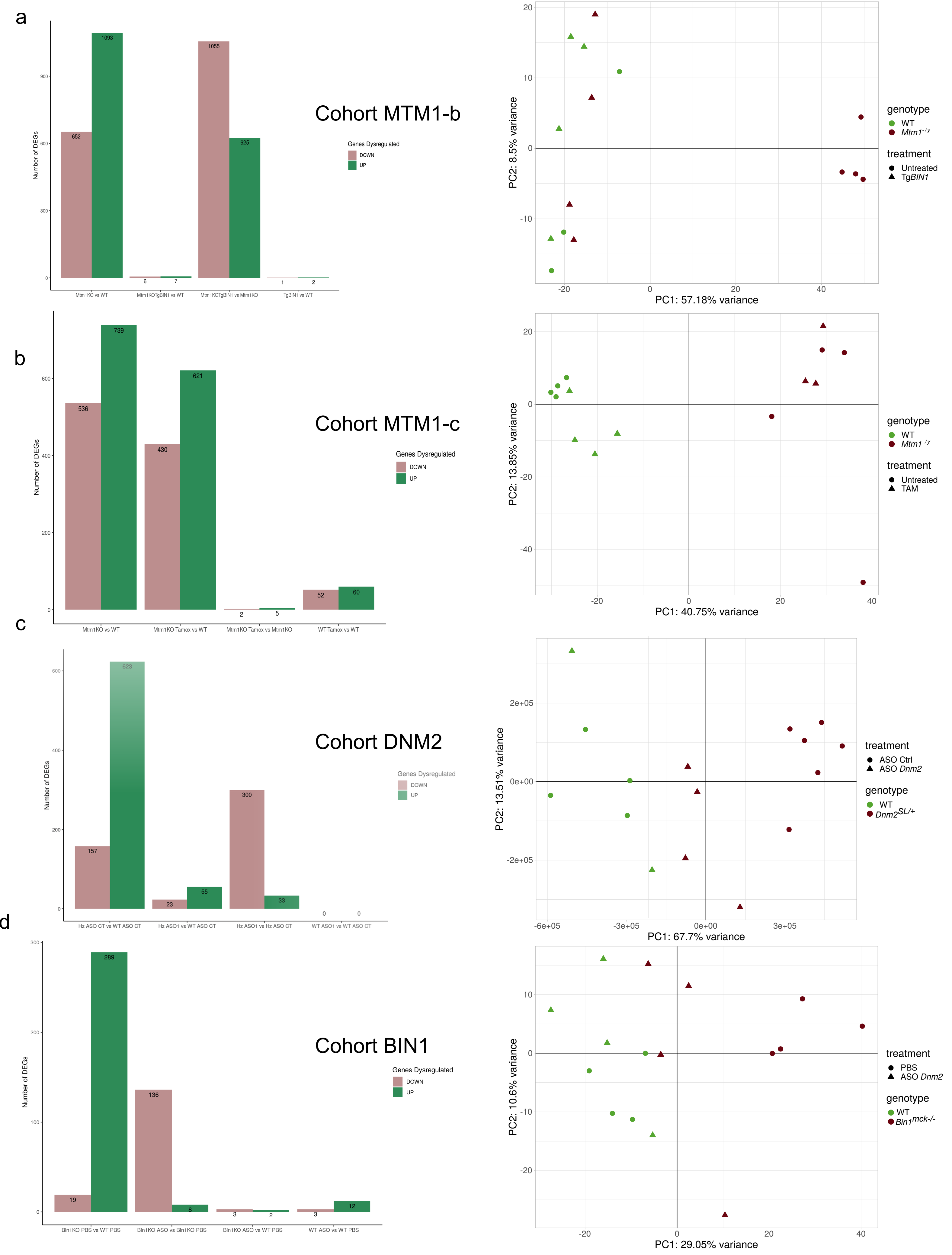

Figure S9. Number of dysregulated genes and the associated PCA for each cohort for four comparisons (Disease vs WT, Disease vs Rescue, Rescue vs Disease, and WT treated vs WT). (a) Cohort MTM1-b. (b) Cohort MTM1-c. (c) Cohort DNM2. (d) Cohort BIN1.

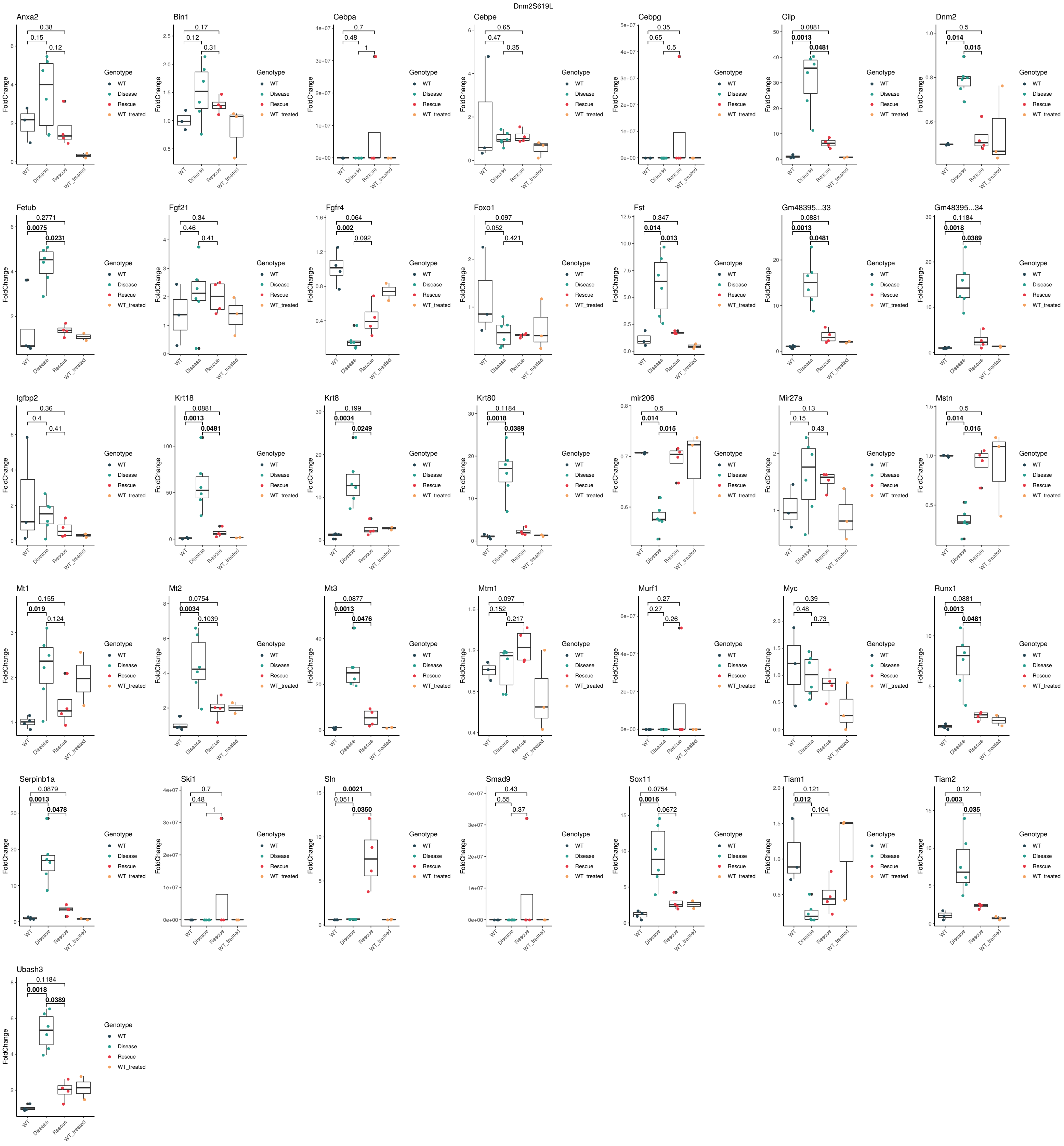

Figure S10. mRNA expression levels of genes of interest in diseased, rescued and control mice in the DNM2 cohort at 7 w. Boxplots displaying normalized Ct values. Pairwise significance calculated by Dunn's test, $p < 0.05$ are represented in bold.

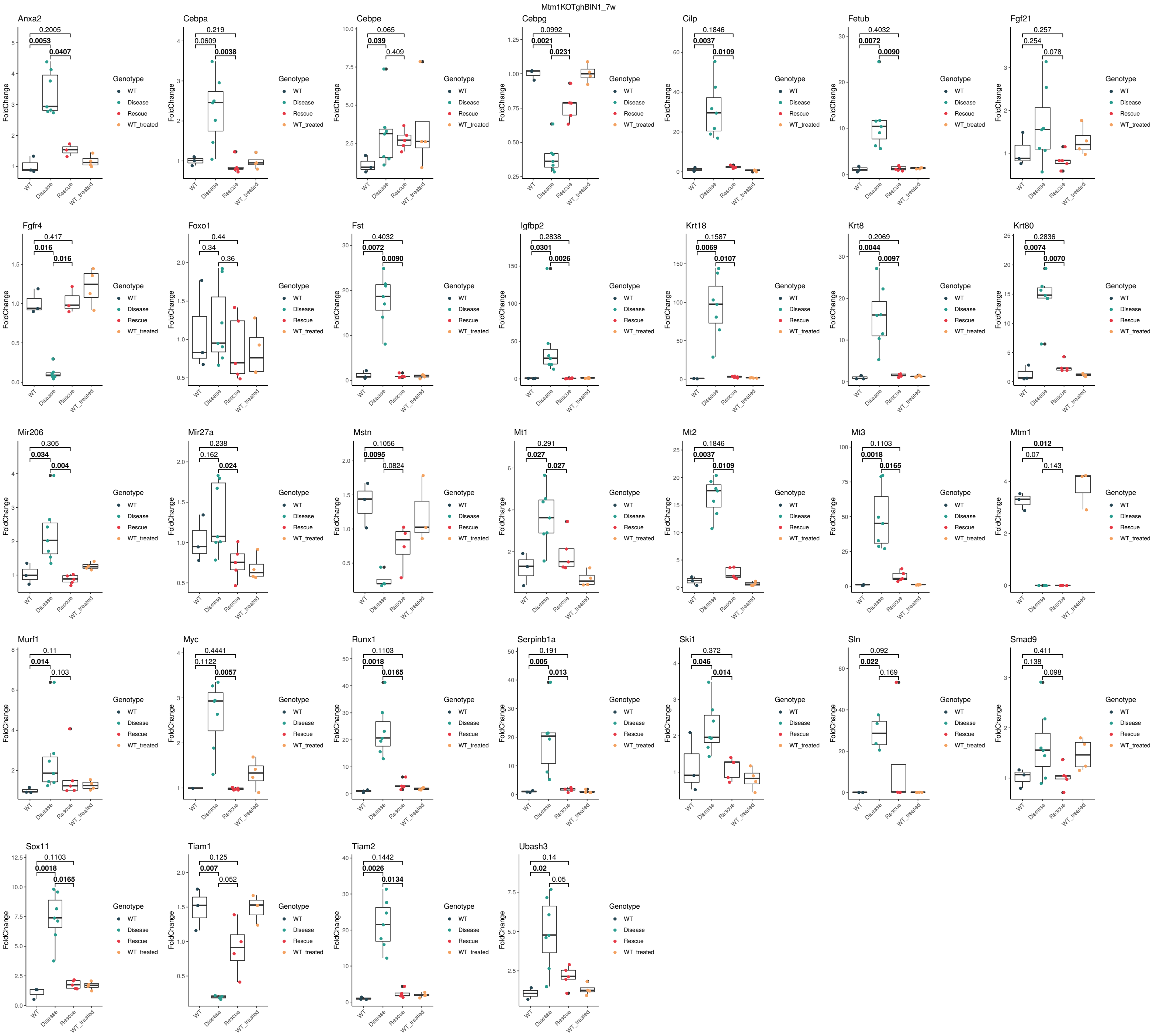

Figure S11. mRNA expression levels of genes of interest in diseased, rescued and control mice in the MTM1-b cohort at 7 w. Boxplots displaying normalized Ct values. Pairwise significance calculated by Dunn’s test, $p < 0.05$ are represented in bold.

Figure S12. mRNA expression levels of genes of interest in diseased, rescued and control mice in the BIN1 cohort at 7 w. Boxplots displaying normalized Ct values. Pairwise significance calculated by Dunn's test, $p < 0.05$ are represented in bold.

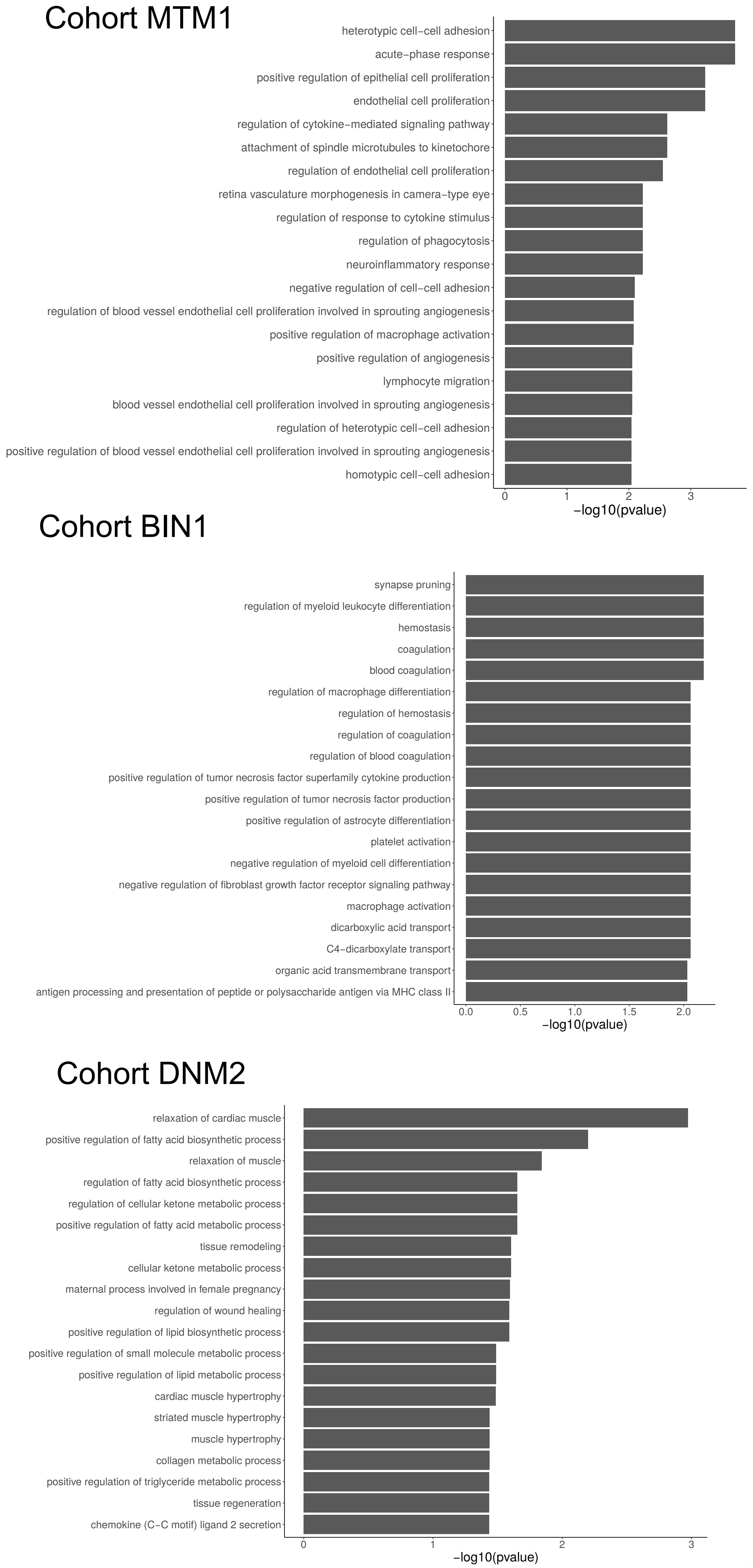

Figure S13. Gene Ontology (GO) enrichment analysis of the specific differentially expressed genes (a) in MTM1 cohort (b) in BIN1 cohort and (c) in DNM2 cohort. The 20 GO biological process terms with the lowest p-value are displayed.

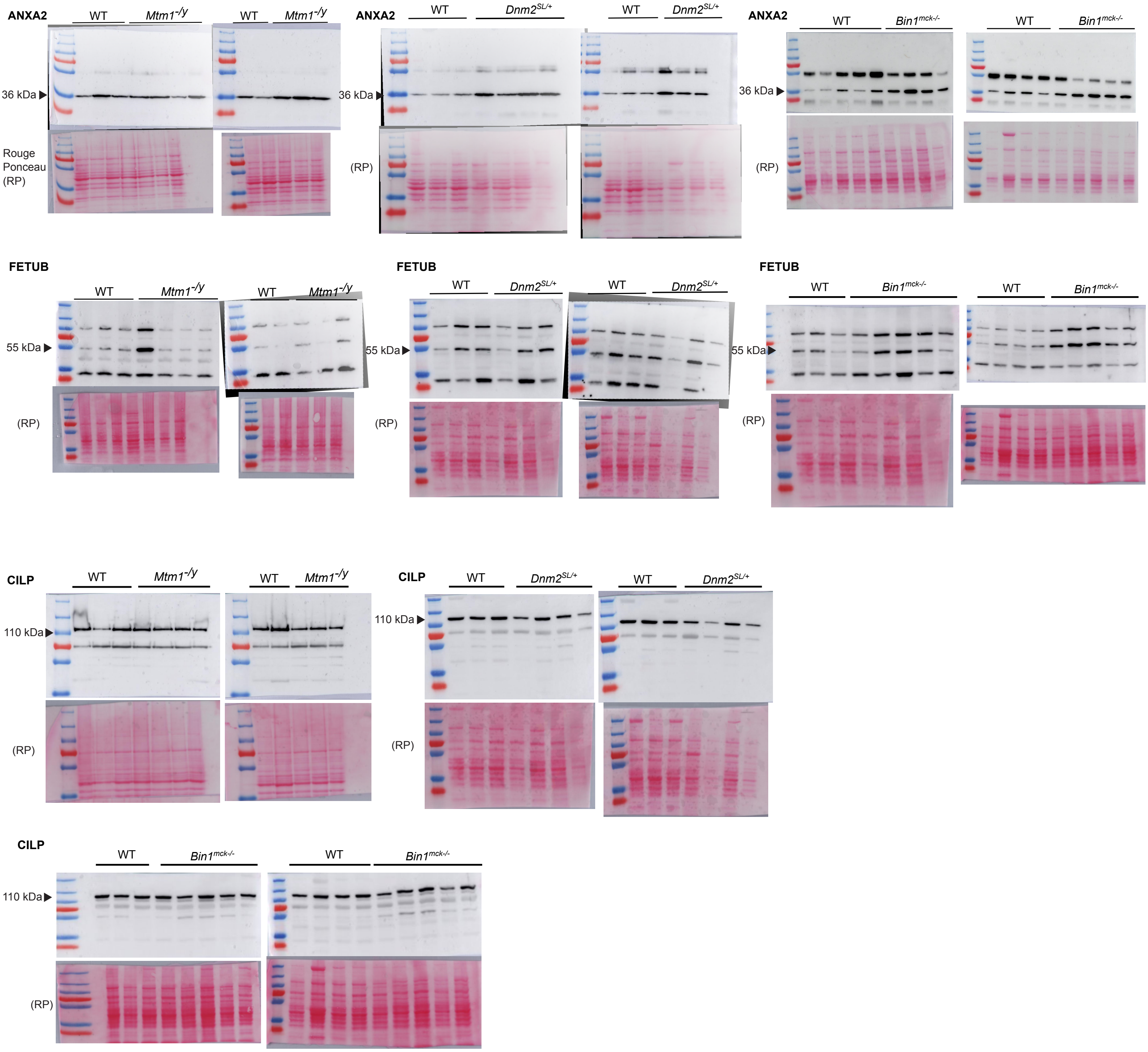

Figure S14. Blot related to Fig 7b.

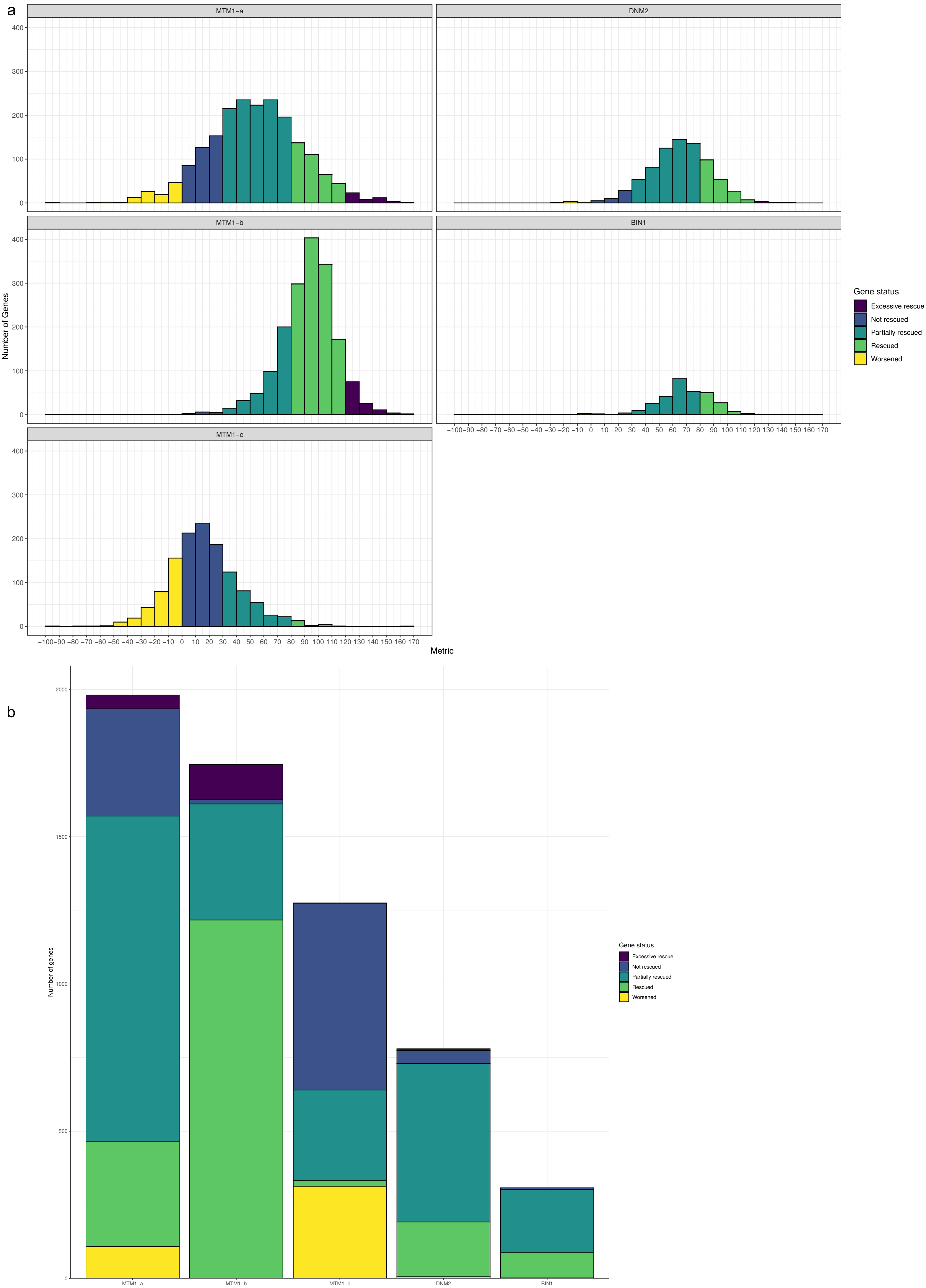
a
MTM1−a
DNM2
MTM1−b
BIN1
MTM1−c
Number of Genes
0
100
200
300
400
−100 −90 −80 −70 −60 −50 −40 −30 −20 −10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170
Metric
Gene status
Excessive rescue
Not rescued
Partially rescued
Rescued
Worsened
b
Number of genes
0
500
1000
1500
2000
MTM1−a
MTM1−b
MTM1−c
DNM2
BIN1
Gene status
Excessive rescue
Not rescued
Partially rescued
Rescued
Worsened

Figure S15. (a) Histogram displaying the proportion of genes according to their status and the metric per cohort. (b) Barplot showing the number of genes dysregulated and the status of these genes through the different therapies.

Table S1. Number of mice included in the different cohorts for transcriptomic and proteomic experiments.

Table S2. List of the 287 genes commonly differentially expressed in MTM1-CNM cohorts (Fig 2a).

Table S3. List of the 632 genes differentially expressed in common for MTM1-a, MTM1-b and MTM1-c cohorts.

Table S4. List of the specific dysregulated genes expressed in MTM1-CNM cohorts (Fig 2c).

Table S5. List of the 68 differentially expressed genes common between mice (Tibialis anterior) and dogs (Vastus Lateralis).

Table S6. List of the 53 differentially expressed genes common between mice (Tibialis anterior) and dogs (Biceps Femoris).

Table S7. List of DEGs in cohort MTM1-a.

Table S8. List of DEP Mtm1−/y vs WT (Cohort MTM1-a)

Table S9. List of the 155 common differentially expressed genes for the MTM1-a, MTM1-b, MTM1-c, DNM2 and BIN1 cohorts.

Table S10. List of DEGs in cohort MTM1-b.

Table S11. List of DEGs in cohort MTM1-c.

Table S12. List of DEGs in cohort DNM2.

Table S13. List of DEGs in cohort BIN1.

Table S14. List of the specific dysregulated genes expressed in MTM1, DNM2 and BIN1 cohorts (Fig 5b).

Table S15. List of the 42 common differentially expressed genes for the MTM1-a, MTM1-b, DNM2 and BIN1 cohorts.

Table S16. List of proteins retrieved by mass spectrometry in serum of WT mice at 8 w.

Table S17. List of primers used for RT-qPCR.