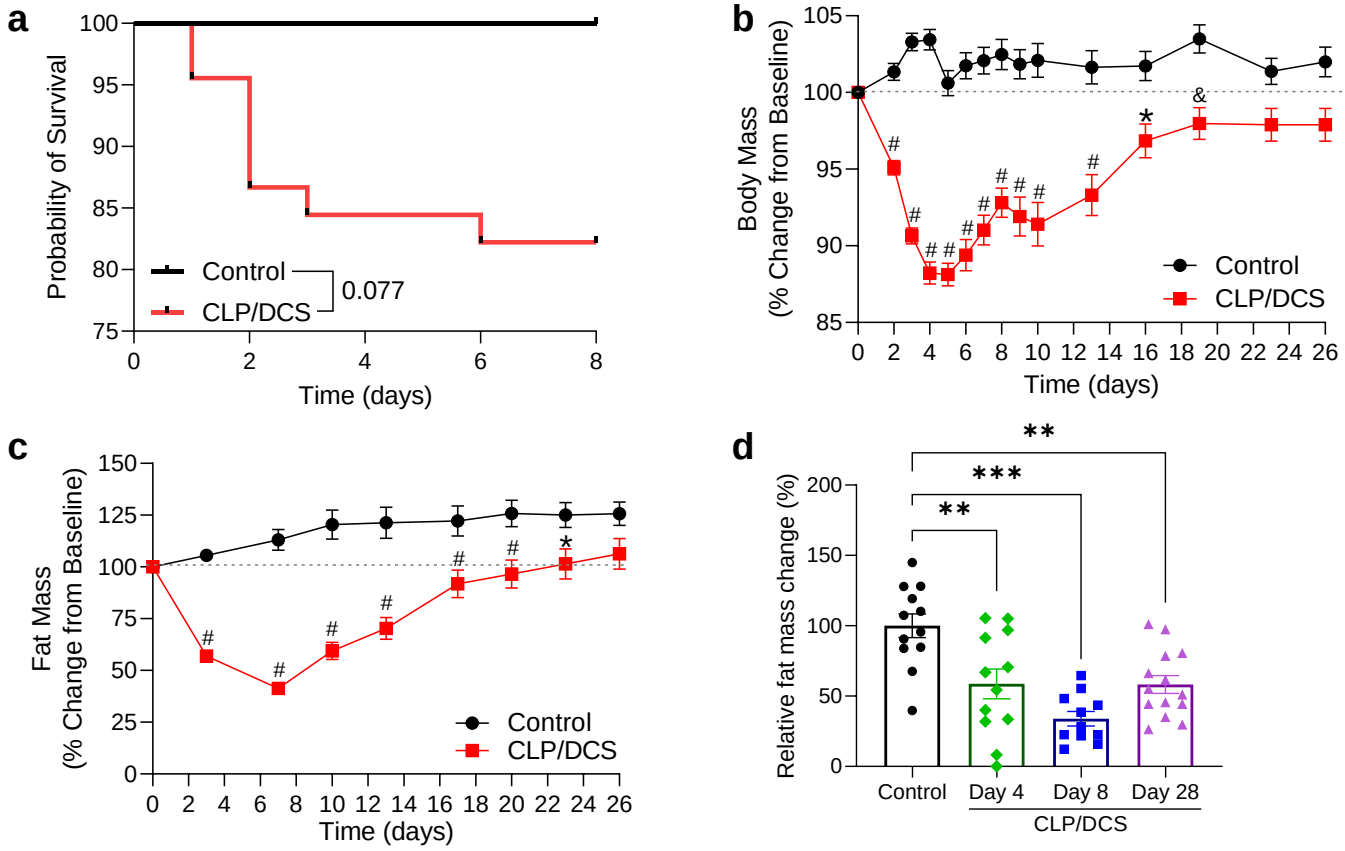
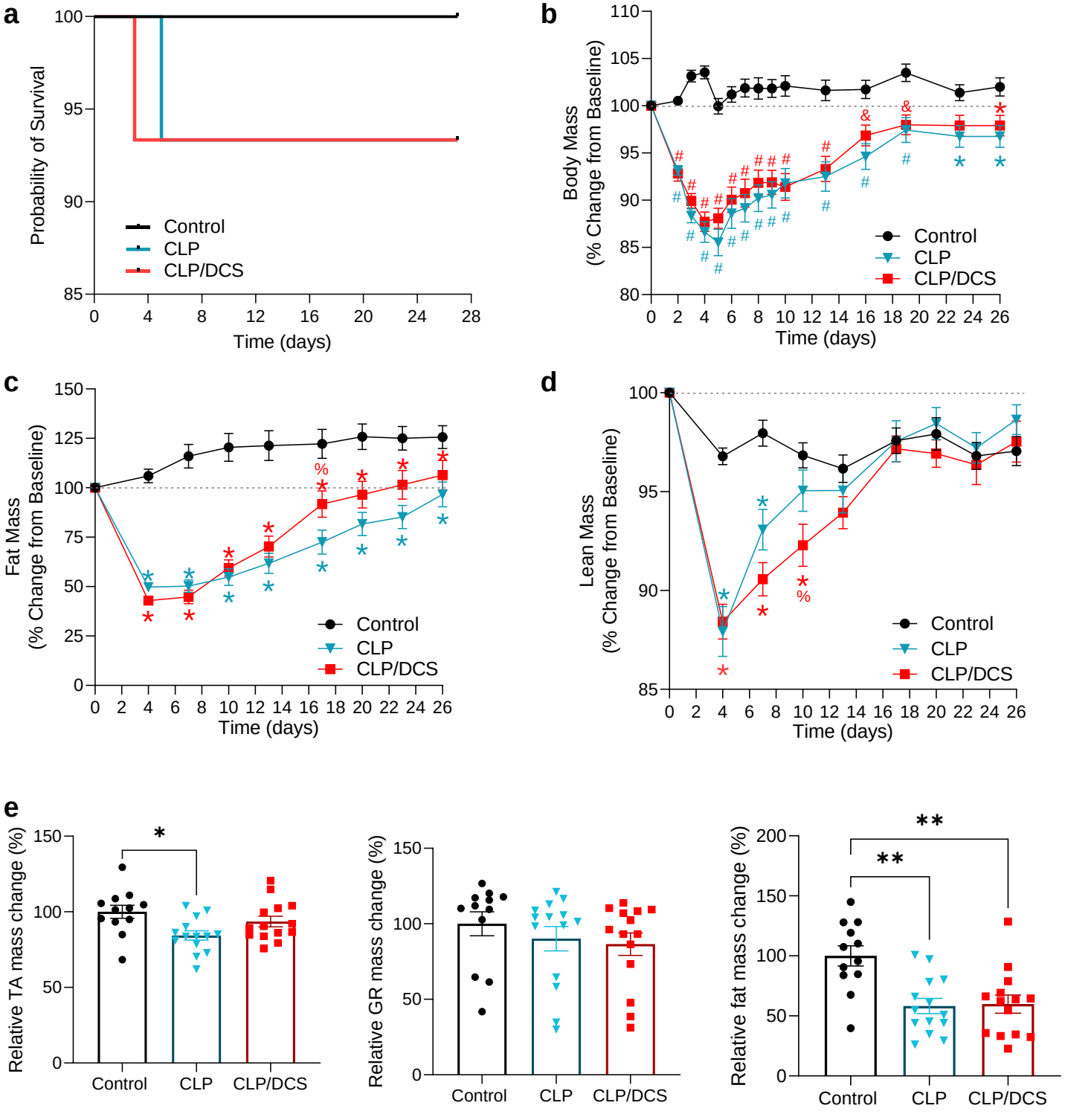
Supplemental Figure 1



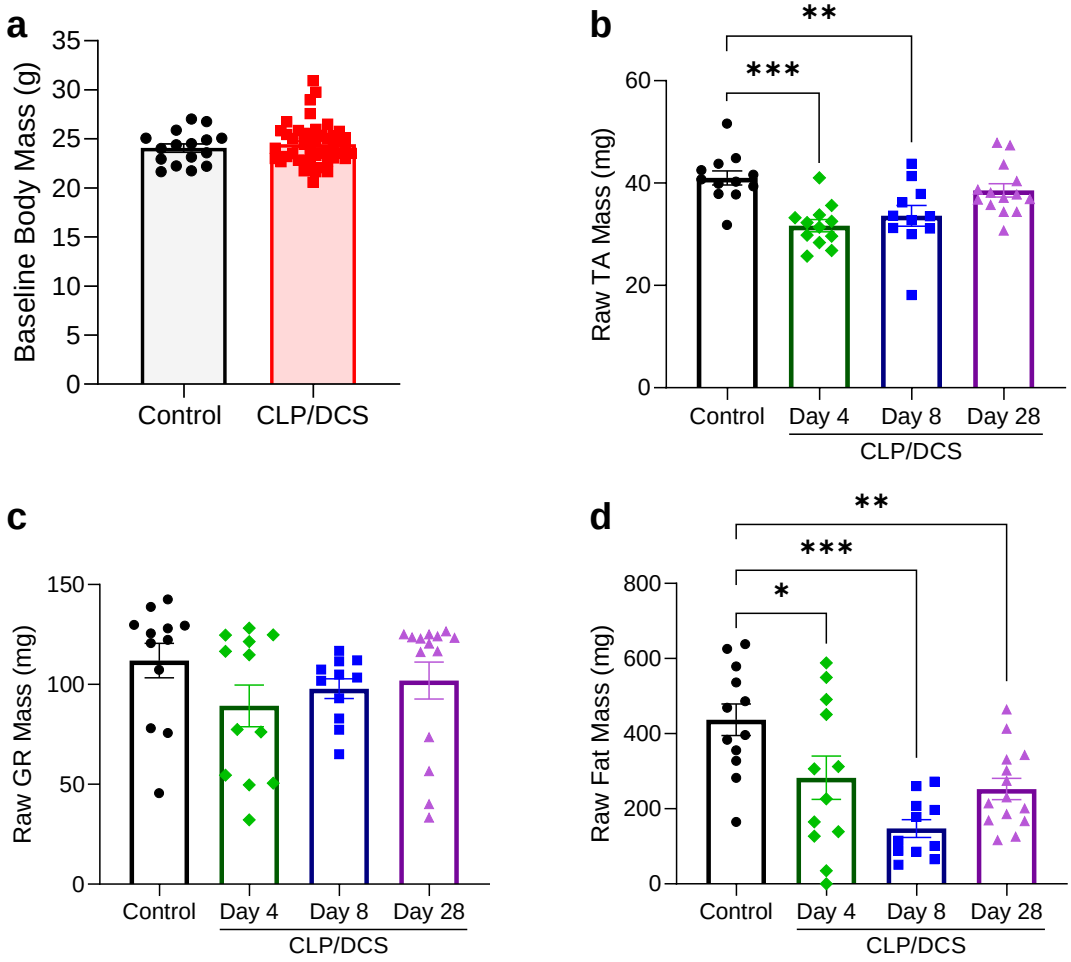
Supplemental Figure 1. Additional characterization of acute survival and fat mass loss in CLP/DCS mice. Combined experiments (A) acute Kaplan-Meier survival for control and CLP/DCS. Control and CLP/DCS data subset is depicted in Figure 1A. (B-C) Control and CLP/DCS percent change from baseline in body weight (B) and fat mass (C). Data from mouse MRI on day 3 or 4 is represented as day 3. (D) Harvested wet weight, as change in percent of control, of fat pad normalized to baseline body weight in control and CLP/DCS day 4, 8, and 28. Data from harvested fat mass on days 27 or 28 is represented on graph as day 28. A = log-rank test. B-C = Two-way ANOVA with Bonferroni multiple comparisons (BMC). D = One-way ANOVA with BMC. Significance: *p<0.05, **/$^{\&}$p<0.01, ***/$^{\#}$p<0.001. A, n = 16-45. B, n = 16-45. C, n =12-14. Each n = one mouse.

Supplemental Figure 2



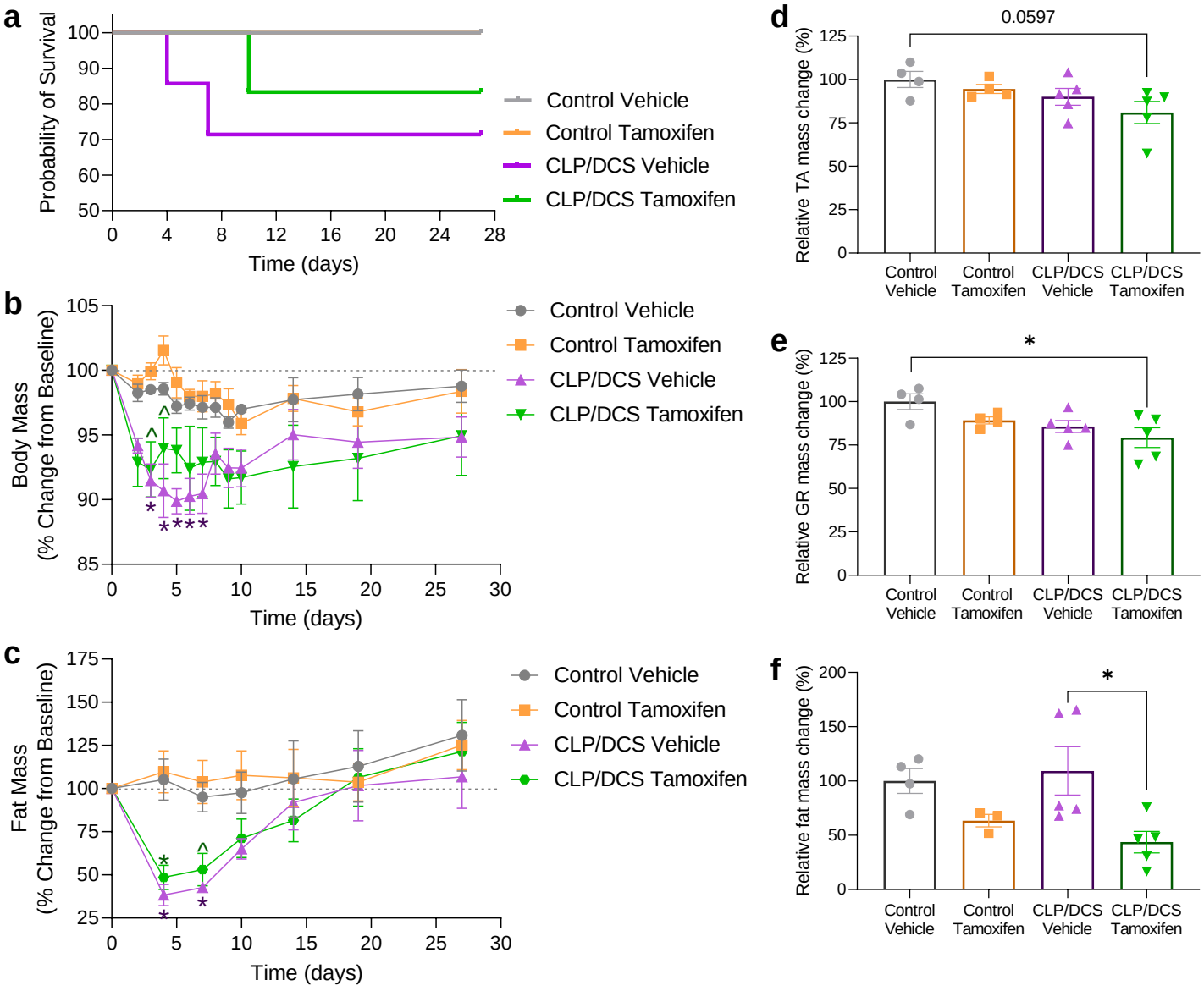
Supplemental Figure 2. Role of CLP versus CLP/DCS in survival, body, lean, and fat mass. (A) Kaplan-Meier survival curve of control, cecal ligation and puncture (CLP), and CLP and daily chronic stress (CLP/DCS) mice to experiment endpoint. (B-D) Control, CLP, and CLP/DCS percent change from baseline in body mass (B), fat mass (C), and lean mass (D). (E) Harvested wet weight, as change in percent of control, of tibialis anterior (TA), gastrocnemius (GR), and fat pad normalized to baseline body weight, respectively, in control, CLP, and CLP/DCS groups. Data from harvested TA, GR, and fat mass on days 27 or 28 is represented on graph as day 28. Control and CLP/DCS data subset is also depicted in Figure 1A and C-D and Supplemental Figure 1B-D. A = log-rank test. B - D = Two-way ANOVA with BMC. E = One-way ANOVA with BMC. B, significance: *$p<0.05$, &$p<0.01$, #$p<0.001$ versus control. C - D, significance: *CLP or CLP/DCS versus control, %CLP versus CLP/CS; see supplemental tables 2 and 3 for all p-value comparisons in panel C and D, respectively. N = 12-16.

Supplemental Figure 3



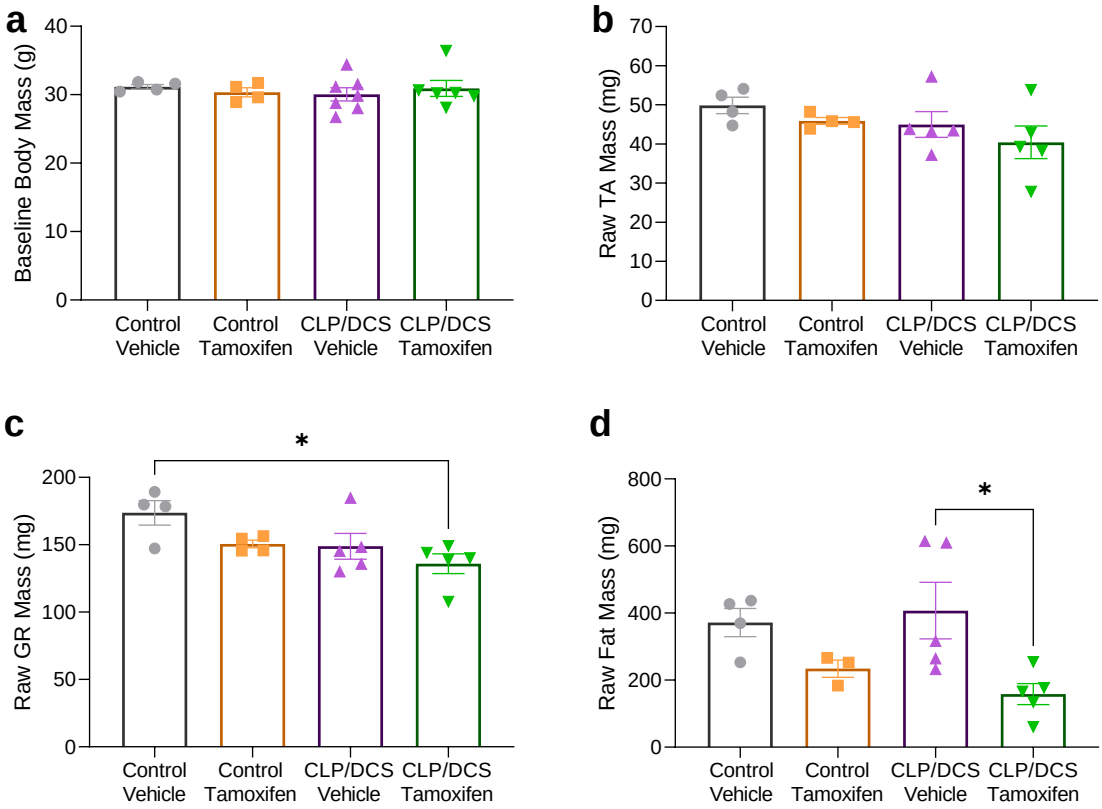
Supplemental Figure 3. Raw muscle and fat masses from control and CLP/DCS mice across time. (A) Baseline body mass between control and all CLP/DCS mice from combined experiments where data is represented in Figure 1, Supplemental Figure 1, and 2. (B-D) Control and CLP/DCS raw mass of harvested TA (B), GR (C), and fat (D). A = Student's unpaired t-test. B – D = One-way ANOVA with BMC. Significance is *p<0.05, **p<0.01, ***p<0.001. A, n = 16-45. B – D, n = 11-14. Each n = one mouse.

Supplemental Figure 4



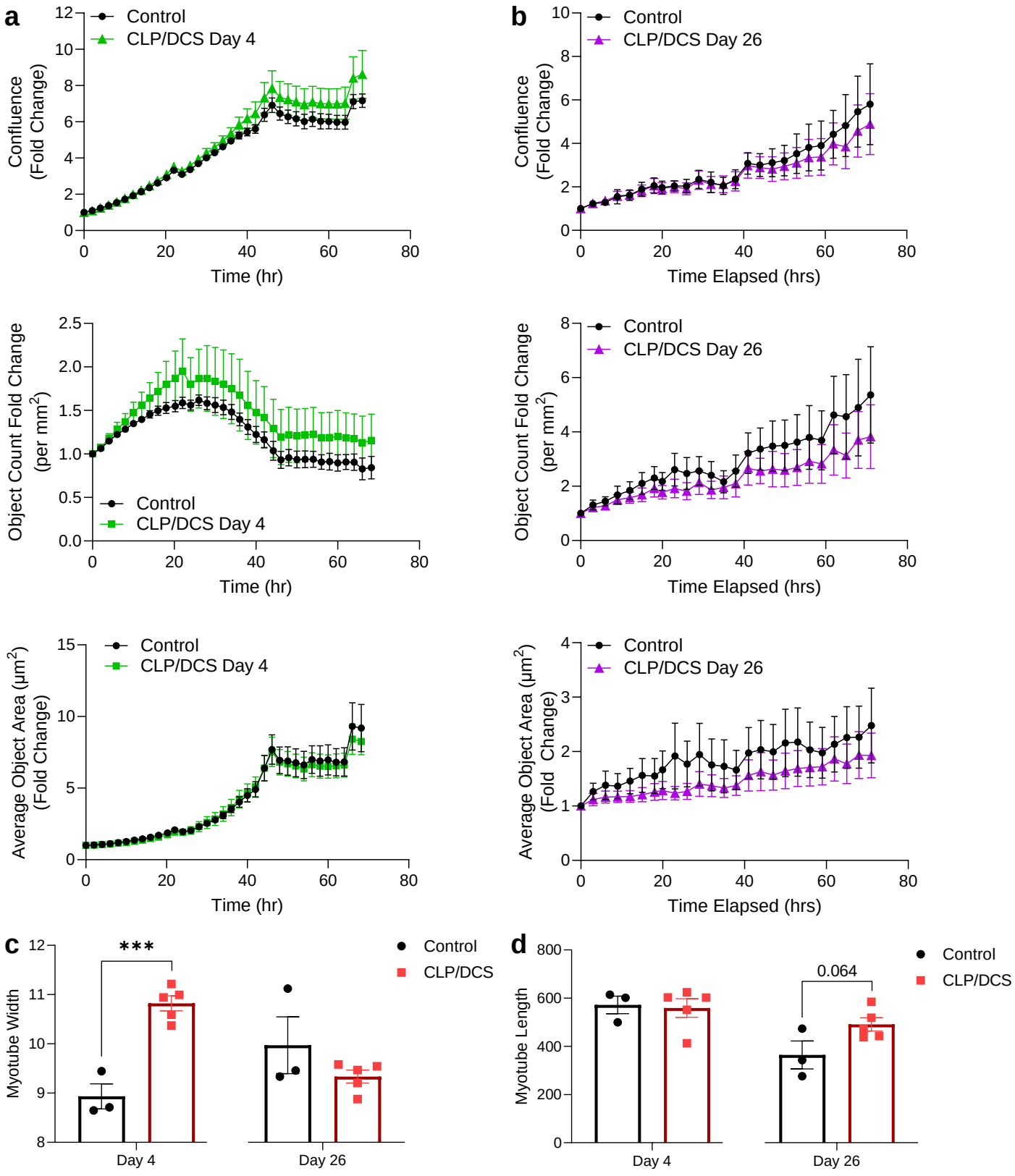
Supplemental Figure 4. Satellite cell reduction during sepsis does not affect mouse fat mass or body weight. (A-F) Pax7-DTA vehicle or tamoxifen treated control or CLP/DCS mice (A) Kaplan-Meier survival curve, (B) percent change in weight from baseline, (C) percent change in fat mass from baseline, and percent change of controls of harvested wet weights normalized to initial body weight of (D) TA, (E) GR, or (F) fat pad. A = log-rank test. B - C = Two-way ANOVA with BMC where: *significant vs. Control Vehicle and Control Tamoxifen and ^significant vs. Control Tamoxifen; n = 4-7. D - F = One-way ANOVA with BMC where significance is *$p<0.05$, **$p<0.01$, ***$p<0.001$; n = 3-5. Each n = one mouse.

Supplemental Figure 5



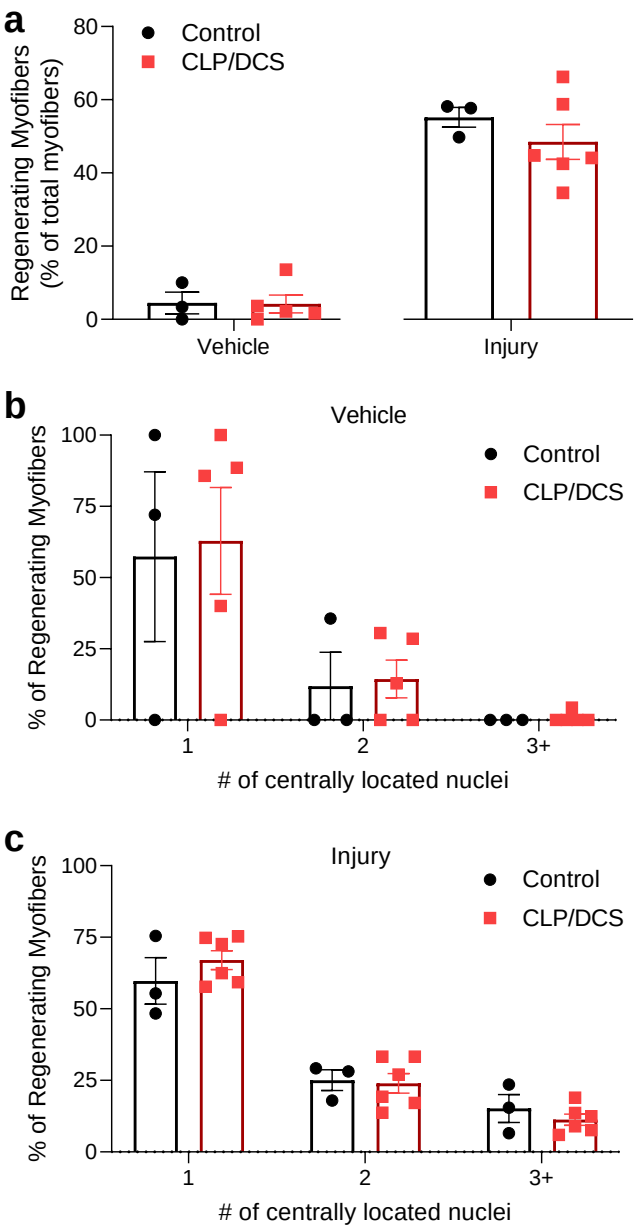
Supplemental Figure 5. Control and CLP/DCS reduction of satellite cell experiment raw muscle and fat masses. (A) Baseline body mass between control and CLP/DCS mice treated with vehicle or tamoxifen. (B-D) Control and CLP/DCS vehicle or tamoxifen treated raw mass of harvested TA (B), GR (C), and fat (D). A - D = One-way ANOVA with BMC where significance is *p<0.05, **p<0.01, ***p<0.001. N = 4-7. Each n = one mouse.

Supplemental Figure 6



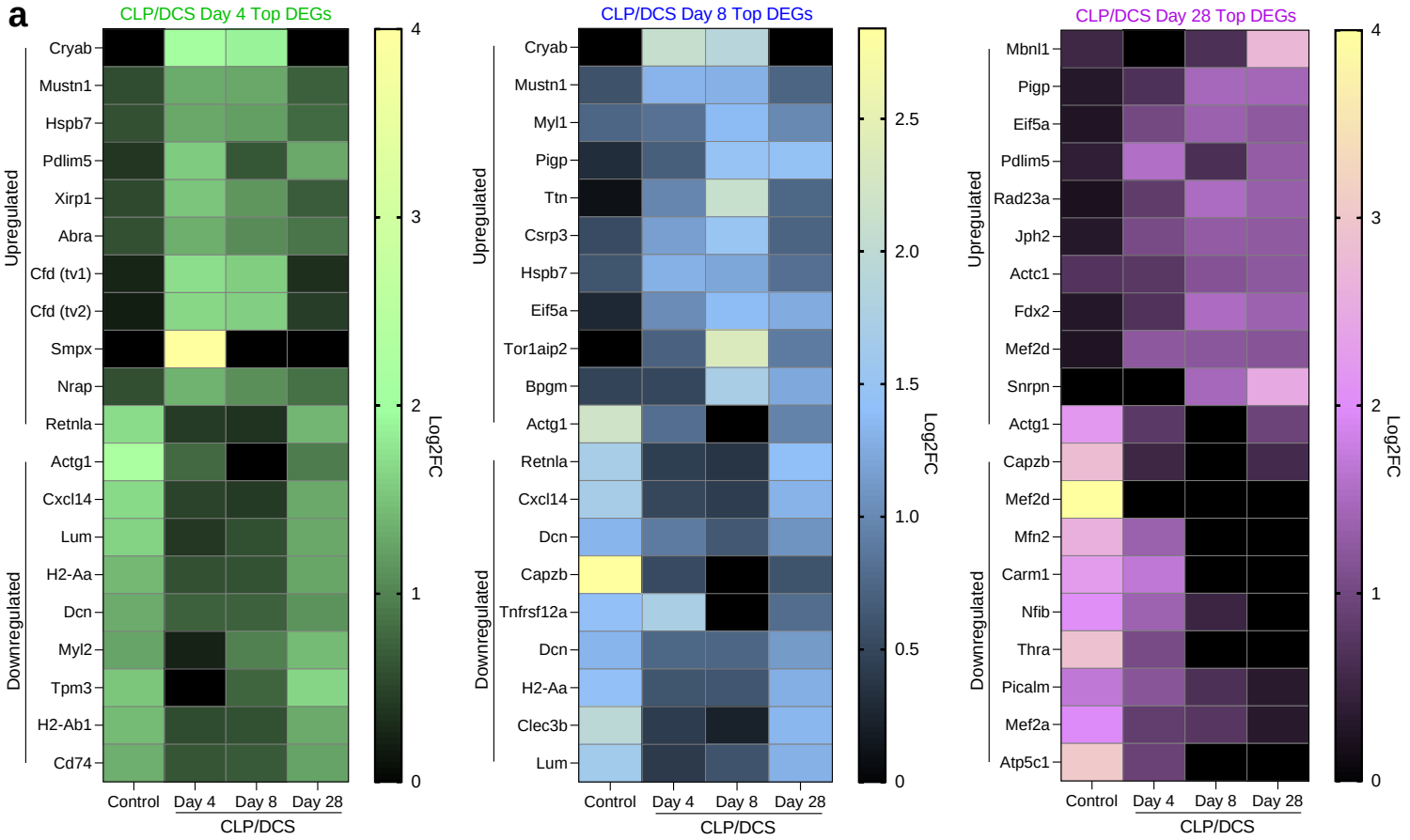
Supplemental Figure 6. Satellite cells isolated from post sepsis mice do not have drastic alterations in their differentiation capacity. (A) Muscle stem cell (MuSC) differentiation in control and 3 days after CLP surgery (day 4). Quantification over time of MuSC (top) confluence, (middle) object count, and (bottom) object area fold changes. (B) Control and day 26 CLP/DCS proliferation measurements of MuSCs, with quantification of (top) confluence, (middle) object count, and (bottom) object area fold changes. (C-D) Myotube width and length from control or CLP/DCS differentiated MuSCs at day 4 or day 26. A - B = Two-way ANOVA with BMC. C - D = Student's unpaired t-test. Significance is *$p<0.05$, **$p<0.01$, ***$p<0.001$. N = 2-5. Each n = satellite cells isolated from a single mouse.

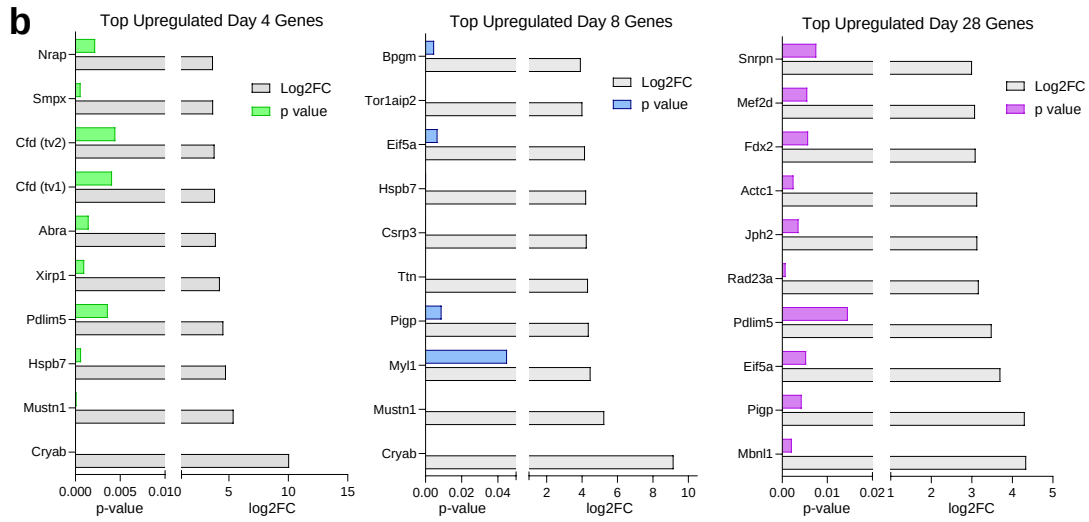
Supplemental Figure 7

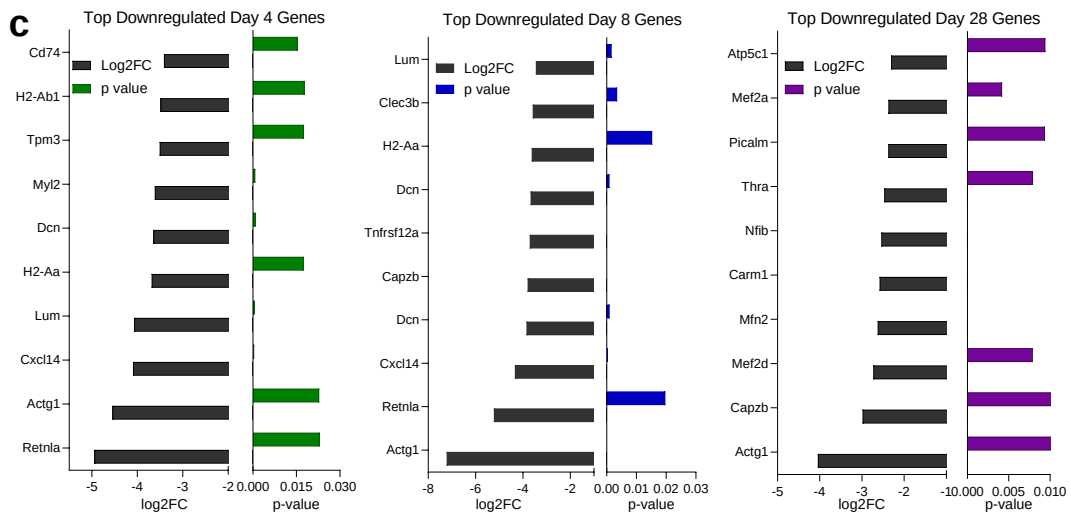


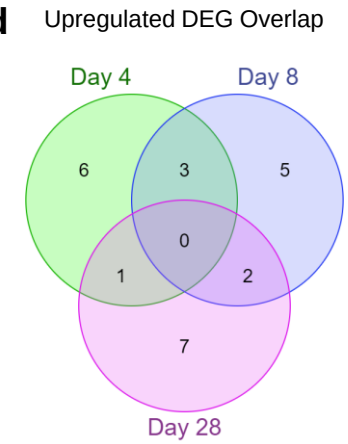
Supplemental Figure 7. The percentage of regenerating myofibers and number of centrally located nuclei are not altered post-second muscle injury in sepsis recovered mice. (A) The percentages of regenerating myofibers in vehicle and injury control or CLP/DCS mice. (B-C) Percentage of regenerating fibers containing 1, 2, or 3+ centrally located nuclei in control and CLP/DCS mice for (B) vehicle treated or (C) injury treated TA's. A - C = Student's unpaired t-test where all values are not significant ($p>0.05$). N = 3-6. Each n = one mouse.

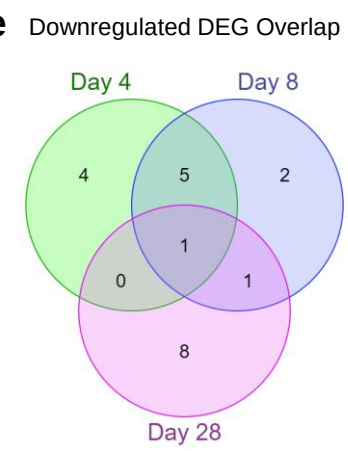
Supplemental Figure 8





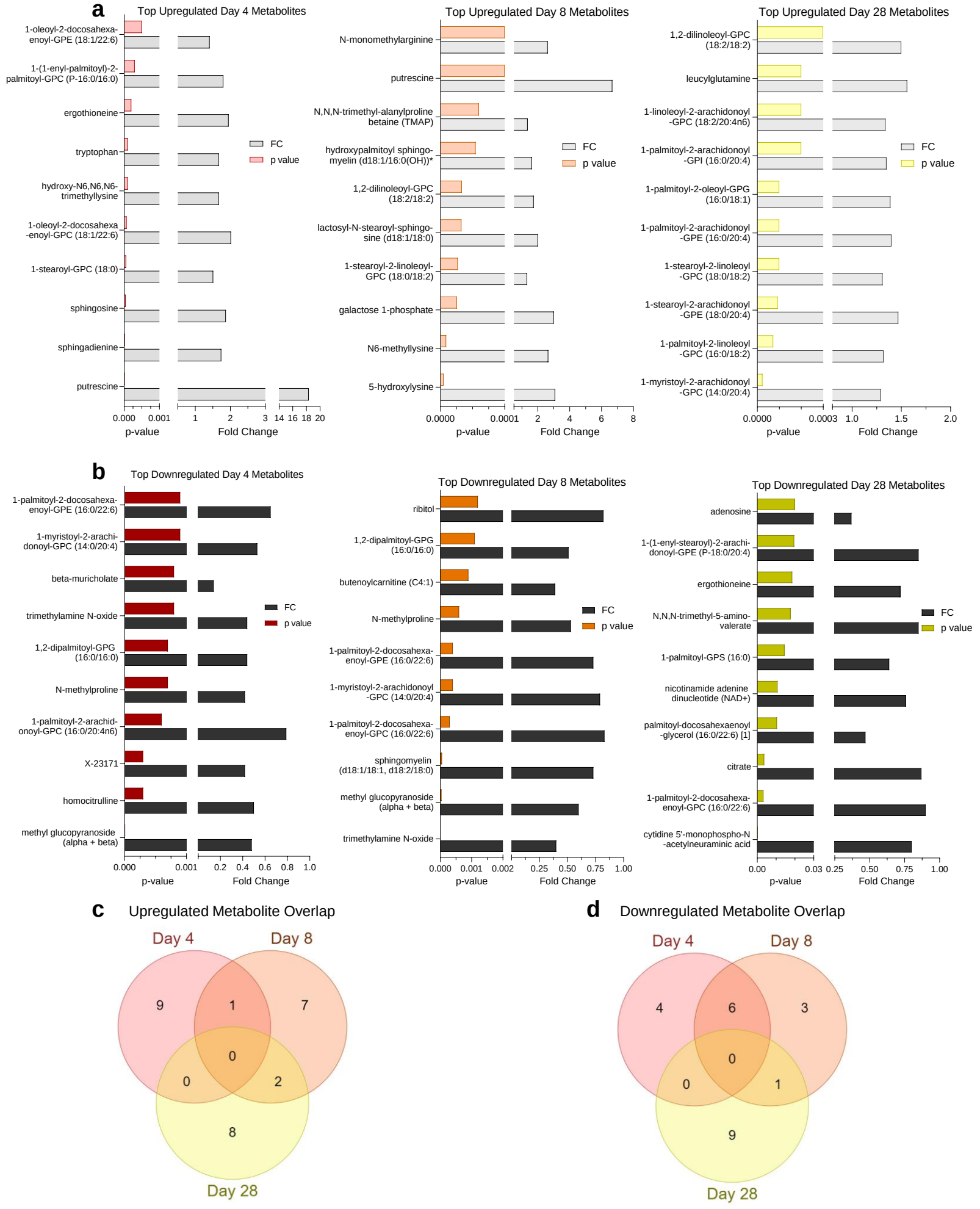






Supplemental Figure 8. Differentially expressed genes in CLP/DCS day 4, 8, and 28 versus control. Combined experimental (A) heatmaps depicting expression of the top ten upregulated and top ten downregulated differentially expressed genes (DEGs) for CLP/DCS day 4, 8, and 28 versus control. (B-C) Log2FC and negative log p-values for top upregulated (B) and downregulated (C) DEGs in CLP/DCS day 4, 8, and 28 versus control from A. (D-E) Venn diagram illustrating the overlapping upregulated (D) or downregulated (E) DEGs in CLP/DCS day 4, 8, and 28 versus control. Each n = pooled satellite cells isolated from 2-3 mice. Satellite cells harvested from mice on day 27 or 28 are labeled as day 28. Top DEGs were defined by: Day 4 = p-value < 0.05 and -1.75 > LOG2FC > 1.75; Day 8 = p-value < 0.05 and -2 > LOG2FC > 2; Day 28 = p-value < 0.05 and -1.25 > LOG2FC > 1.25.

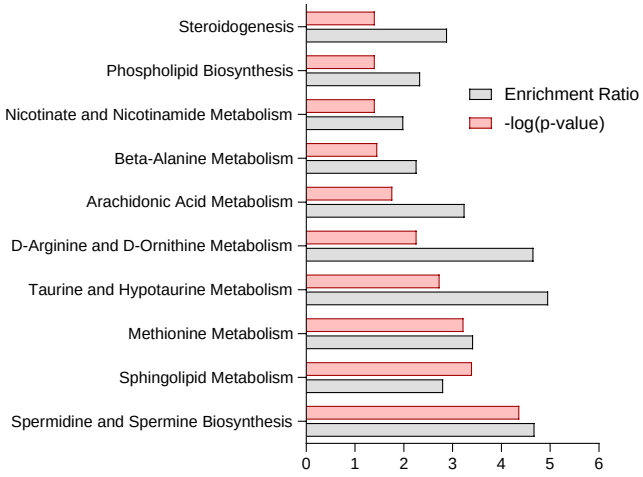
Supplemental Figure 9



Supplemental Figure 9. Metabolite changes in gastrocnemius from CLP/DCS day 4, 8, and 28 versus control. Combined experimental (A-B) scaled intensity fold change and p-values for the top ten upregulated (A) and top ten downregulated (B) metabolites in whole GR muscle from CLP/DCS day 4, 8, and 28 versus control. (C-D) Venn diagram illustrating the overlapping upregulated (C) or downregulated (D) top altered metabolites from A in CLP/DCS day 4, 8, and 28 versus control. GRs that were harvested on day 27 or 28 are labeled as day 28. Top metabolites determined via Student's unpaired t-test with Welch's correction (Metabolon), $p<0.05$. N = 6 per group. Each n = one mouse.

Supplemental Figure 10

a



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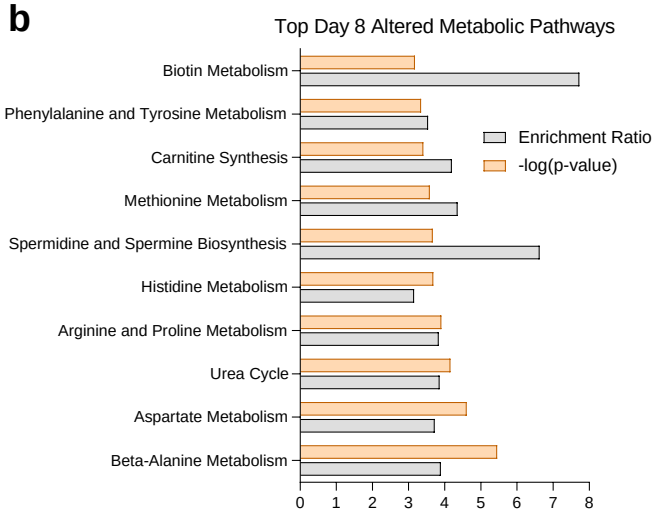
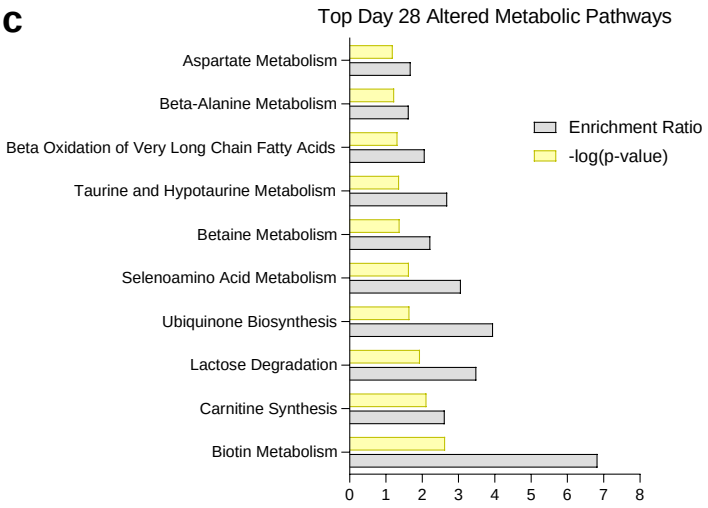
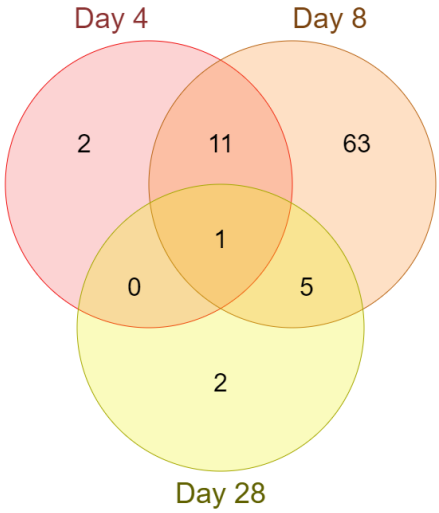


c



d



Supplemental Figure 10. Longitudinal altered metabolic pathways in post-CLP/DCS mice gastrocnemius. Combined experimental (A-C) top altered metabolic pathways enrichment ratios and negative log p-values from GR CLP/DCS day 4 (A), day 8 (B), and day 28 (C) versus control. (D) Venn diagram depicting overlapping top altered metabolic pathways. GRs that were harvested on day 27 or 28 are labeled as day 28. N = 6 per group. Each n = one mouse.

Supplemental Tables

P-values	Control	Day 4	Day 8	Day 26- 28
Control		0.4093	0.0021	0.4691
Day 4	0.4093		0.0111	0.9023
Day 8	0.0021	0.0111		0.0078
Day 26-28	0.4691	0.9023	0.0078	

Supplemental Table 1. p-values from nonlinear fit pairwise comparisons of minimum feret diameter means from control, day 4, day 8, and day 28 myofibers from figure 1E.

Time	Comparison	Adjusted p-value
Day 4	Control vs. CLP	<0.0001
	Control vs. CLP/DCS	<0.0001
	CLP vs. CLP/DCS	>0.9999
Day 7	Control vs. CLP	<0.0001
	Control vs. CLP/DCS	<0.0001
	CLP vs. CLP/DCS	>0.9999
Day 10	Control vs. CLP	<0.0001
	Control vs. CLP/DCS	<0.0001
	CLP vs. CLP/DCS	>0.9999
Day 13	Control vs. CLP	<0.0001
	Control vs. CLP/DCS	<0.0001
	CLP vs. CLP/DCS	0.7314
Day 17	Control vs. CLP	<0.0001
	Control vs. CLP/DCS	0.0002
	CLP vs. CLP/DCS	0.0269
Day 20	Control vs. CLP	<0.0001
	Control vs. CLP/DCS	0.0005
	CLP vs. CLP/DCS	0.1302
Day 23	Control vs. CLP	<0.0001
	Control vs. CLP/DCS	0.0065
	CLP vs. CLP/DCS	0.0809
Day 26	Control vs. CLP	0.0005
	Control vs. CLP/DCS	0.0361
	CLP vs. CLP/DCS	0.5489

Supplemental Table 2. Longitudinal fat mass p-values from two-way ANOVA with BMC between control, CLP, and CLP/DCS from supplementary figure 2C.

Time	Comparison	Adjusted p-value
Day 4	Control vs. CLP	<0.0001
	Control vs. CLP/DCS	<0.0001
	CLP vs. CLP/DCS	>0.9999
Day 7	Control vs. CLP	0.0002
	Control vs. CLP/DCS	<0.0001
	CLP vs. CLP/DCS	0.0896
Day 10	Control vs. CLP	0.4154
	Control vs. CLP/DCS	0.0005
	CLP vs. CLP/DCS	0.0499
Day 13	Control vs. CLP	>0.9999
	Control vs. CLP/DCS	0.1933
	CLP vs. CLP/DCS	0.9850
Day 17	Control vs. CLP	>0.9999
	Control vs. CLP/DCS	>0.9999
	CLP vs. CLP/DCS	>0.9999
Day 20	Control vs. CLP	>0.9999
	Control vs. CLP/DCS	>0.9999
	CLP vs. CLP/DCS	0.5624
Day 23	Control vs. CLP	>0.9999
	Control vs. CLP/DCS	>0.9999
	CLP vs. CLP/DCS	>0.9999
Day 26	Control vs. CLP	0.5578
	Control vs. CLP/DCS	>0.9999
	CLP vs. CLP/DCS	>0.9999

Supplemental Table 3. Longitudinal lean mass p-values from two-way ANOVA with BMC between control, CLP, and CLP/DCS from supplementary figure 2D.

Time	Comparison	Adjusted p-value
Day 4	Control Vehicle vs. Control Tamoxifen	>0.9999
	Control Vehicle vs. CLP/DCS Vehicle	0.0034
	Control Vehicle vs. CLP/DCS Tamoxifen	<0.0001
	Control Tamoxifen vs. CLP/DCS Vehicle	0.0007
	Control Tamoxifen vs. CLP/DCS Tamoxifen	<0.0001
	CLP/DCS Vehicle vs. CLP/DCS Tamoxifen	0.6269
Day 7	Control Vehicle vs. Control Tamoxifen	>0.9999
	Control Vehicle vs. CLP/DCS Vehicle	0.0296
	Control Vehicle vs. CLP/DCS Tamoxifen	0.0002
	Control Tamoxifen vs. CLP/DCS Vehicle	0.0171
	Control Tamoxifen vs. CLP/DCS Tamoxifen	0.0001
	CLP/DCS Vehicle vs. CLP/DCS Tamoxifen	0.9821
Day 10	Control Vehicle vs. Control Tamoxifen	>0.9999
	Control Vehicle vs. CLP/DCS Vehicle	0.9318
	Control Vehicle vs. CLP/DCS Tamoxifen	0.0011
	Control Tamoxifen vs. CLP/DCS Vehicle	>0.9999
	Control Tamoxifen vs. CLP/DCS Tamoxifen	0.0052
	CLP/DCS Vehicle vs. CLP/DCS Tamoxifen	0.0629
Day 14	Control Vehicle vs. Control Tamoxifen	>0.9999
	Control Vehicle vs. CLP/DCS Vehicle	>0.9999
	Control Vehicle vs. CLP/DCS Tamoxifen	0.0015
	Control Tamoxifen vs. CLP/DCS Vehicle	>0.9999
	Control Tamoxifen vs. CLP/DCS Tamoxifen	0.0080
	CLP/DCS Vehicle vs. CLP/DCS Tamoxifen	0.0665
Day 19	Control Vehicle vs. Control Tamoxifen	>0.9999
	Control Vehicle vs. CLP/DCS Vehicle	0.4899
	Control Vehicle vs. CLP/DCS Tamoxifen	0.0032
	Control Tamoxifen vs. CLP/DCS Vehicle	>0.9999
	Control Tamoxifen vs. CLP/DCS Tamoxifen	0.0231
	CLP/DCS Vehicle vs. CLP/DCS Tamoxifen	0.3374
Day 27	Control Vehicle vs. Control Tamoxifen	>0.9999
	Control Vehicle vs. CLP/DCS Vehicle	>0.9999
	Control Vehicle vs. CLP/DCS Tamoxifen	0.0277
	Control Tamoxifen vs. CLP/DCS Vehicle	>0.9999
	Control Tamoxifen vs. CLP/DCS Tamoxifen	0.0884
	CLP/DCS Vehicle vs. CLP/DCS Tamoxifen	0.2441

Supplemental Table 4. Longitudinal p-values from two-way ANOVA with BMC of lean mass between control vehicle, control tamoxifen, CLP/DCS vehicle, and CLP/DCS tamoxifen from figure 2B.

P-values	Control Vehicle	Control Tamoxifen	CLP/DCS Vehicle	CLP/DCS Tamoxifen
Control Vehicle		0.2448	0.3057	0.0066
Control Tamoxifen	0.2448		0.0191	0.0558
CLP/DCS Vehicle	0.3057	0.0191		0.0001
CLP/DCS Tamoxifen	0.0066	0.0558	0.0001	

Supplemental Table 5. p-values from nonlinear fit pairwise comparisons of minimum feret diameter means from control vehicle, control tamoxifen, CLP/DCS vehicle, and CLP/DCS tamoxifen myofibers from figure 2C.

P-values	Control Vehicle	Control Injured	CLP/DCS Vehicle	CLP/DCS Injured
Control Vehicle		0.3072	0.7802	0.0003
Control Injured	0.3072		0.5016	0.0029
CLP/DCS Vehicle	0.7802	0.5016		0.0015
CLP/DCS Injured	0.0003	0.0029	0.0015	

Supplemental Table 6. p-values from nonlinear fit pairwise comparisons of minimum feret diameter means from control vehicle, control injured, CLP/DCS vehicle, and CLP/DCS injured myofibers from figure 4B.

Ingenuity Canonical Pathways	-log(p-value)	Ratio	z-score
Polyamine Regulation in Colon Cancer	23	0.403	#NUM!
FAT10 Signaling Pathway	22.8	0.429	#NUM!
BAG2 Signaling Pathway	19.2	0.298	#NUM!
Protein Ubiquitination Pathway	17.1	0.142	#NUM!
Inhibition of ARE-Mediated mRNA Degradation Pathway	12.9	0.161	1
Huntington's Disease Signaling	11.4	0.114	#NUM!
Hepatic Fibrosis / Hepatic Stellate Cell Activation	10.2	0.129	#NUM!
p38 MAPK Signaling	6.32	0.127	1.941
Atherosclerosis Signaling	5.77	0.115	#NUM!
Actin Cytoskeleton Signaling	5.65	0.0857	1.069
Calcium Signaling	5.33	0.088	0.707
ILK Signaling	5.28	0.0909	0.775
Dilated Cardiomyopathy Signaling Pathway	5.14	0.103	0.277
Glycogen Biosynthesis II (from UDP-D-Glucose)	4.81	0.571	1
Agranulocyte Adhesion and Diapedesis	4.27	0.0794	#NUM!
PAK Signaling	4.19	0.102	0.333
Neuroprotective Role of THOP1 in Alzheimer's Disease	4.19	0.102	-1.667
Glucocorticoid Receptor Signaling	4.13	0.0551	#NUM!
Tumor Microenvironment Pathway	4.1	0.0838	-1.069
ERK5 Signaling	3.97	0.125	1.414
ERK/MAPK Signaling	3.75	0.0748	1.387
Cholecystokinin/Gastrin-mediated Signaling	3.52	0.0924	0.333
Sertoli Cell-Sertoli Cell Junction Signaling	3.43	0.0728	#NUM!
HIF1α Signaling	3.38	0.0721	0
Cardiac Hypertrophy Signaling	3.3	0.0659	0.535

Supplemental Table 7. Top 25 altered pathways from IPA analysis of RNA sequencing data from CLP/DCS day 4 post-septic satellite cells versus control (DEGs: p-value < 0.05 and -1.75 > LOG2FC > 1.75).

Ingenuity Canonical Pathways	-log(p-value)	Ratio	z-score
Oxidative Phosphorylation	49.7	0.536	7.421
Mitochondrial Dysfunction	48.6	0.409	#NUM!
Sirtuin Signaling Pathway	22.3	0.202	-3.162
Estrogen Receptor Signaling	17.7	0.156	2.263
Glucocorticoid Receptor Signaling	16.2	0.129	#NUM!
Calcium Signaling	9.93	0.157	3.441
Dilated Cardiomyopathy Signaling Pathway	8.92	0.178	-1.606
TCA Cycle II (Eukaryotic)	8.76	0.458	3.317
Glycolysis I	7.31	0.4	3.162
Gluconeogenesis I	7.31	0.4	3.162
Protein Ubiquitination Pathway	7.18	0.124	#NUM!
ILK Signaling	6.69	0.136	1.877
Hepatic Fibrosis / Hepatic Stellate Cell Activation	6.32	0.134	#NUM!
Huntington's Disease Signaling	6	0.114	1.134
Cellular Effects of Sildenafil (Viagra)	5.58	0.141	#NUM!
Actin Cytoskeleton Signaling	5.36	0.114	3.273
HIF1α Signaling	5.24	0.12	2.041
Agranulocyte Adhesion and Diapedesis	4.55	0.112	#NUM!
Role of NFAT in Cardiac Hypertrophy	4.35	0.109	3.273
Amyotrophic Lateral Sclerosis Signaling	4.33	0.139	0.905
Netrin Signaling	4.16	0.167	2.309
Cardiac Hypertrophy Signaling	4.08	0.101	3.13
Hypoxia Signaling in the Cardiovascular System	4.04	0.162	0.447
Aspartate Degradation II	3.92	0.571	2
Integrin Signaling	3.69	0.103	3.441

Supplemental Table 8. Top 25 altered pathways from IPA analysis of RNA sequencing data from CLP/DCS day 8 post-septic satellite cells versus control (DEGs: p-value < 0.05 and -2 > LOG2FC > 2).

Ingenuity Canonical Pathways	-log(p-value)	Ratio	z-score
Oxidative Phosphorylation	59.1	0.527	7.353
Mitochondrial Dysfunction	58.7	0.398	#NUM!
Sirtuin Signaling Pathway	27.3	0.185	-4.11
Estrogen Receptor Signaling	20.4	0.134	2.6
Calcium Signaling	12.7	0.144	3.71
Glucocorticoid Receptor Signaling	11.2	0.0861	#NUM!
Glycolysis I	10.5	0.44	3.317
Gluconeogenesis I	10.5	0.44	3.317
TCA Cycle II (Eukaryotic)	9.3	0.417	3.162
Dilated Cardiomyopathy Signaling Pathway	8.86	0.144	-0.535
Role of NFAT in Cardiac Hypertrophy	8.24	0.114	4.264
Dopamine-DARPP32 Feedback in cAMP Signaling	7.18	0.116	2.138
Cellular Effects of Sildenafil (Viagra)	5.83	0.114	#NUM!
Cardiac β-adrenergic Signaling	5.51	0.103	-0.577
Synaptic Long Term Potentiation	5.32	0.116	2.138
Cardiac Hypertrophy Signaling	5.19	0.0853	3.638
nNOS Signaling in Skeletal Muscle Cells	5.1	0.188	#NUM!
Senescence Pathway	4.72	0.0774	3.3
Glycogen Biosynthesis II (from UDP-D-Glucose)	4.65	0.571	#NUM!
3-phosphoinositide Degradation	4.47	0.0904	2.887
HIF1α Signaling	4.45	0.0865	3.771
White Adipose Tissue Browning Pathway	4.4	0.103	3.207
D-myo-inositol-5-phosphate Metabolism	4.36	0.0885	2.887
Protein Kinase A Signaling	4.33	0.0672	1.279
D-myo-inositol (1,4,5,6)-Tetrakisphosphate Biosynthesis	4.27	0.0909	2.714

Supplemental Table 9. Top 25 altered pathways from IPA analysis of RNA sequencing data from day 28 post-septic satellite cells versus control (DEGs: p-value < 0.05 and -1.25 > LOG2FC > 1.25).