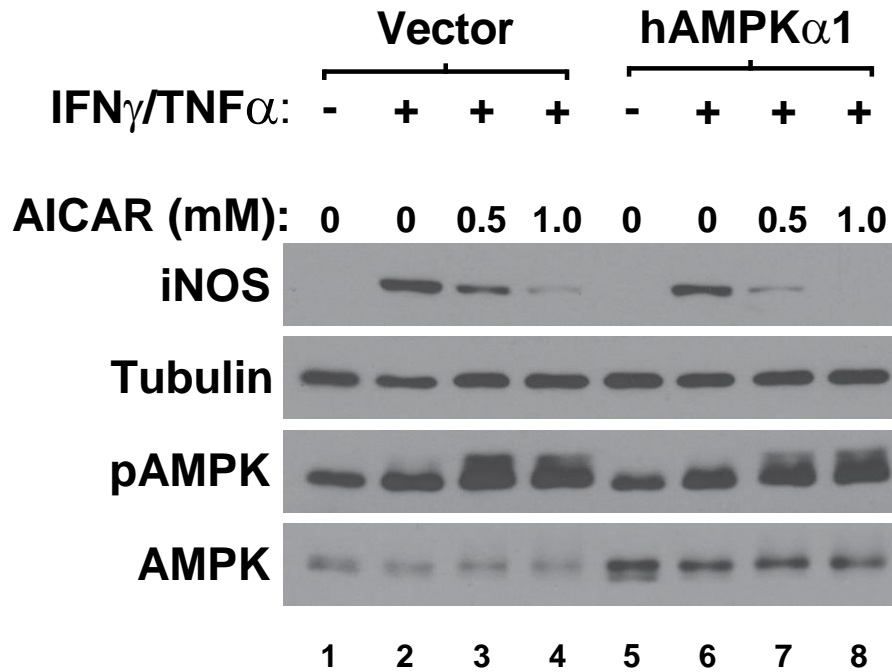


Appendix

The AMPK agonist 5-Aminoimidazole-4-carboxamide ribonucleotide (AICAR), but not metformin, prevents inflammation-associated cachectic muscle wasting

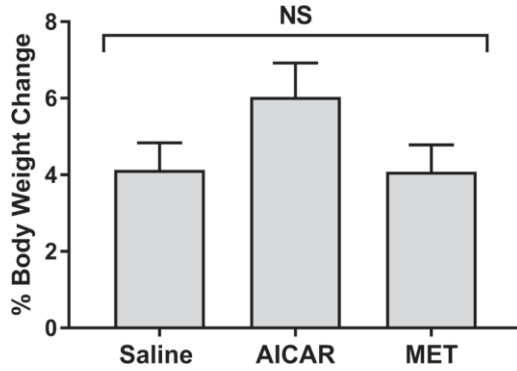
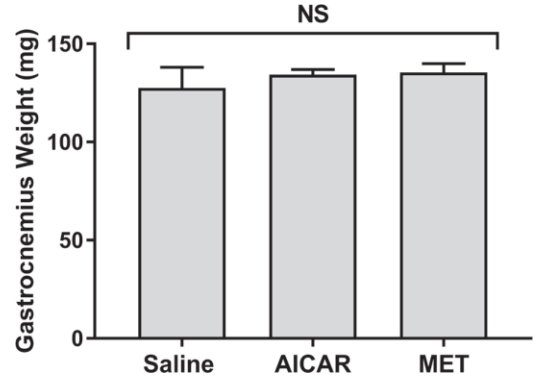
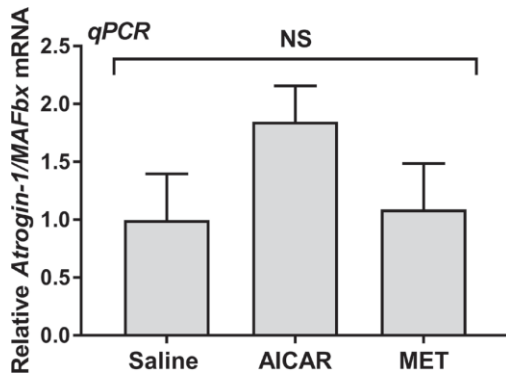
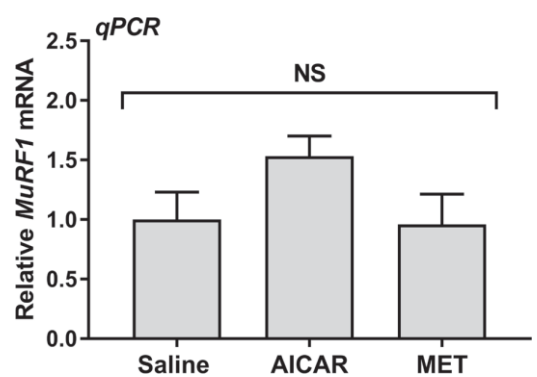
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Table of Content	... 1
Appendix Figure S1. Overexpression of AMPK α increases C2C12 sensitivity to AICAR	... 2
Appendix Figure S2. Consecutive daily AICAR or metformin treatment does not affect body weight or muscle mass.	... 3
Appendix Figure S3. Single doses of AICAR or metformin alone do not affect body weight or muscle mass.	... 4
Appendix Table S1. qPCR Primer Sequences	... 5
Appendix Table S2. Figure 1 Significance p-values	... 6
Appendix Table S3. Figure 2 Significance p-values	... 7
Appendix Table S4. Figure 3 Significance p-values	... 8
Appendix Table S5. Figure 4 Significance p-values	... 8
Appendix Table S6. Figure 5 Significance p-values	... 9-10
Appendix Table S7. Figure 6 Significance p-values	... 11
Appendix Table S8. Figure 7 Significance p-values	... 12-14
Appendix Table S9. Figure 8 Significance p-values	... 15
Appendix Table S10. Figure 9 Significance p-values	... 15
Appendix Table S11. Figure EV3 Significance p-values	... 16
Appendix Table S12. Figure EV4 Significance p-values	... 16
Appendix Table S13. Figure EV5 Significance p-values	... 17
Appendix Table S14. Table 1 Significance p-values	... 18
Appendix Table S14. Table 2 Significance p-values	... 19



Appendix Figure S1. Overexpression of AMPK α increases C2C12 sensitivity to AICAR.

C2C12 myoblast cells were transfected with constructs expressing human AMPK α 1 (hAMPK α 1) or an empty vector negative control (Vector). Cells were then treated with IFN γ /TNF α and the indicated doses of AICAR. Western blot analysis performed for protein levels of iNOS, tubulin, and phosphor-Thr172-AMPK (pAMPK), and total AMPK.

A**B****C****D**

Appendix Figure S2. Consecutive daily AICAR or metformin treatment does not affect body weight or muscle mass.

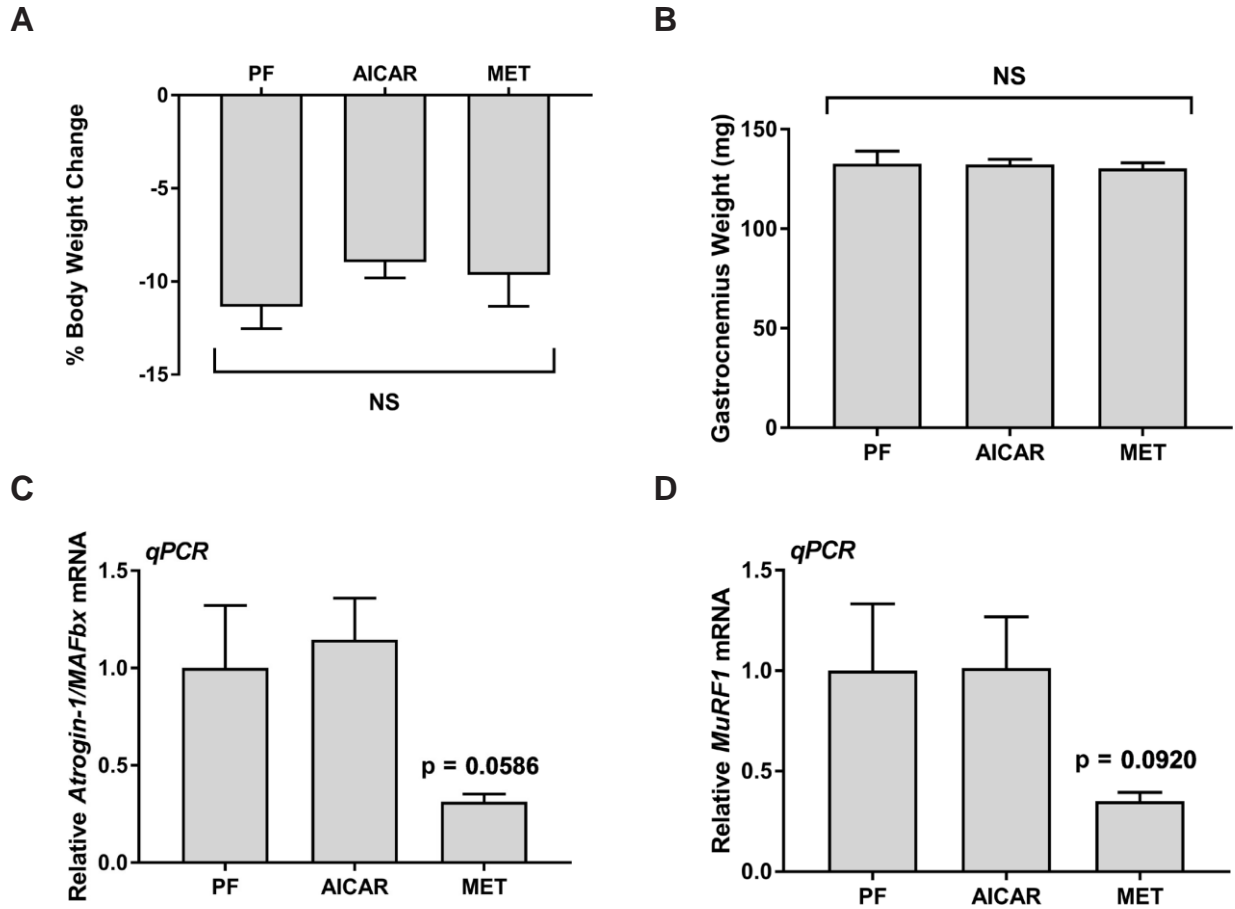
BALB/C mice were intraperitoneally injected daily with AICAR ($500\text{mg kg}^{-1}\text{ day}^{-1}$), metformin ($250\text{mg kg}^{-1}\text{ day}^{-1}$), or an equivalent volume of saline for 7-9 days.

(A) Percent body weight change.

(B) Gastrocnemius muscle weights.

(C-D) RT-qPCR analysis of Atrogin-1/MAFbx (C) and MuRF1 (D) mRNA expression from the tibialis anterior.

Data information: Results are derived from four mice per cohort ($n = 4$) and error bars represent the SEM. Significance between means was determined using ANOVA. NS, not significant.



Appendix Figure S3. Single doses of AICAR or metformin alone do not affect body weight or muscle mass.

C57Bl/6 mice were intraperitoneally injected with either AICAR (500mg kg⁻¹), metformin (250mg kg⁻¹), or an equivalent volume of saline. All cohorts were pair-fed (PF) to the food consumption rate of LPS injected mice. Tissue samples were collected 18h later.

(A) Percent body weight change.

(B) Gastrocnemius muscle weights.

(C-D) RT-qPCR analysis of Atrogin-1/MAFbx (C) and MuRF1 (D) mRNA expression from the tibialis anterior.

Data information: Results are derived from four mice per cohort (n = 4) and error bars represent the SEM. Significance between means was first determined using ANOVA. Significance p-values were calculated using Fisher's LSD. NS, not significant.

Appendix Table S1. qPCR Primer Sequences.

Gene	Protein	Gene ID	Forward Primer (5'-3')	Reverse Primer (5'-3')
<i>Nos2</i>	iNOS	18126	GTGCGCATGGCTCGGGATGT	GGCTGTCAGAGCCTCGTGGC
<i>Gapdh</i>	GAPDH	14433	AAGGTCATCCCAGAGCTGAA	AGGAGACAACCTGGTCCTCA
<i>Myod1</i>	MyoD	17927	CGACACCGCCTACTACAGTG	TTCTGTGTCGCTTAGGGATG
<i>Myog</i>	Myogenin	17928	CTACAGGCCTTGCTCAGCTC	AGATTGTGGGCGTCTGTAGG
<i>Fbxo3</i>	Atrogin-1 /MAFbx	67731	GACCGGCTACTGTGGAAGAG	CCAGGAGAGAATGTGGCAGT
<i>Trim63</i>	MuRF1	433766	GAGCAAGGCTTTGAGAACATGGACT	GCGTCCAGAGCGTGTCTCACT

Appendix Table S2. Figure 1 Significance p-values.

Figure	Panel	Control	Treatment	p-value	Symbol
1	A, pAMPK/AMPK	NT	AICAR	0.0026	**
1	A, pAMPK/AMPK	NT	MET	< 0.0001	**
1	A, pAMPK/AMPK	NT	IFN γ /TNF α	< 0.0001	**
1	A, pAMPK/AMPK	NT	IFN γ /TNF α + AICAR	0.0003	**
1	A, pAMPK/AMPK	NT	IFN γ /TNF α + MET	0.0002	**
1	A, pAMPK/AMPK	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0923	-
1	A, pAMPK/AMPK	IFN γ /TNF α	IFN γ /TNF α + MET	0.1301	-
1	A, pACC/ACC	NT	AICAR	0.0013	**
1	A, pACC/ACC	NT	MET	0.0247	*
1	A, pACC/ACC	NT	IFN γ /TNF α	0.0015	**
1	A, pACC/ACC	NT	IFN γ /TNF α + AICAR	0.0010	**
1	A, pACC/ACC	NT	IFN γ /TNF α + MET	0.0342	*
1	A, pACC/ACC	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.7911	-
1	A, pACC/ACC	IFN γ /TNF α	IFN γ /TNF α + MET	0.1180	-
1	C	NT	AICAR	0.4964	-
1	C	NT	MET	0.0287	*
1	C	NT	IFN γ /TNF α	0.0033	**
1	C	NT	IFN γ /TNF α + AICAR	0.9965	-
1	C	NT	IFN γ /TNF α + MET	0.0009	**
1	C	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0033	-
1	C	IFN γ /TNF α	IFN γ /TNF α + MET	0.4991	-
1	D	NT	AICAR	0.0047	**
1	D	NT	MET	0.1318	-
1	D	NT	IFN γ /TNF α	< 0.0001	**
1	D	NT	IFN γ /TNF α + AICAR	0.0002	**
1	D	NT	IFN γ /TNF α + MET	< 0.0001	**
1	D	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0004	††
1	D	IFN γ /TNF α	IFN γ /TNF α + MET	0.9299	-
1	E	NT	AICAR	0.6955	-
1	E	NT	MET	0.9582	-
1	E	NT	IFN γ /TNF α	0.0062	**
1	E	NT	IFN γ /TNF α + AICAR	0.7342	-
1	E	NT	IFN γ /TNF α + MET	0.0059	**
1	E	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0118	-
1	E	IFN γ /TNF α	IFN γ /TNF α + MET	0.9791	-

Abbreviations: NT, non-treated. MET, metformin.

Appendix Table S3. Figure 2 Significance p-values.

Figure	Panel	Control	Treatment	p-value	Symbol
2	A	NT	AICAR	0.7561	-
2	A	NT	MET	0.0165	*
2	A	NT	IFN γ /TNF α	0.0025	**
2	A	NT	IFN γ /TNF α + AICAR	0.4003	-
2	A	NT	IFN γ /TNF α + MET	0.0005	**
2	A	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0125	-
2	A	IFN γ /TNF α	IFN γ /TNF α + MET	0.4025	-
2	B	NT	AICAR	0.9267	-
2	B	NT	MET	0.0208	*
2	B	NT	IFN γ /TNF α	0.0025	**
2	B	NT	IFN γ /TNF α + AICAR	0.1200	-
2	B	NT	IFN γ /TNF α + MET	0.0019	**
2	B	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0549	-
2	B	IFN γ /TNF α	IFN γ /TNF α + MET	0.8694	-

Abbreviations: NT, non-treated. MET, metformin.

Appendix Table S4. Figure 3 Significance p-values.

Figure	Panel	Control	Treatment	p-value	Symbol
3	A, pS6K/S6K	NT	AICAR	0.0954	-
3	A, pS6K/S6K	NT	MET	0.1038	-
3	A, pS6K/S6K	NT	IFN γ /TNF α	<0.0001	**
3	A, pS6K/S6K	NT	IFN γ /TNF α + AICAR	0.0380	*
3	A, pS6K/S6K	NT	IFN γ /TNF α + MET	<0.0001	**
3	A, pS6K/S6K	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0005	++
3	A, pS6K/S6K	IFN γ /TNF α	IFN γ /TNF α + MET	0.8461	-
3	A, pS6/S6	NT	AICAR	0.8372	-
3	A, pS6/S6	NT	MET	0.8911	-
3	A, pS6/S6	NT	IFN γ /TNF α	0.0372	*
3	A, pS6/S6	NT	IFN γ /TNF α + AICAR	0.7753	-
3	A, pS6/S6	NT	IFN γ /TNF α + MET	0.0435	*
3	A, pS6/S6	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0205	-
3	A, pS6/S6	IFN γ /TNF α	IFN γ /TNF α + MET	0.9382	-
3	B	NT	AICAR	0.7810	-
3	B	NT	MET	0.1265	-
3	B	NT	IFN γ /TNF α	0.0007	**
3	B	NT	IFN γ /TNF α + AICAR	0.1411	-
3	B	NT	IFN γ /TNF α + MET	0.0001	**
3	B	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0119	-
3	B	IFN γ /TNF α	IFN γ /TNF α + MET	0.2845	-

Abbreviations: NT, non-treated. MET, metformin.

Appendix Table S5. Figure 4 Significance p-values.

Figure	Panel	Control	Treatment	p-value	Symbol
4	A	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0005	++
4	A	IFN γ /TNF α	IFN γ /TNF α + MET	0.3321	-
4	B	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0014	++
4	B	IFN γ /TNF α	IFN γ /TNF α + MET	0.3702	-
4	C	IFN γ /TNF α	IFN γ /TNF α + AICAR	<0.0001	++
4	C	IFN γ /TNF α	IFN γ /TNF α + MET	0.1597	-
4	D	siCTL + IFN γ /TNF α + AICAR 0.5mM	siAMPK + IFN γ /TNF α + AICAR 0.5mM	0.0071	**
4	D	siCTL + IFN γ /TNF α + AICAR 1.0mM	siAMPK + IFN γ /TNF α + AICAR 1.0mM	0.0206	*

Abbreviations: MET, metformin.

Appendix Table S6. Figure 5 Significance p-values.

Figure	Panel	Control	Treatment	p-value	Symbol
5	A, pAMPK/AMPK	NT	AICAR	0.0203	*
5	A, pAMPK/AMPK	NT	CC	0.9541	-
5	A, pAMPK/AMPK	NT	CC + AICAR	0.0217	*
5	A, pACC/ACC	NT	AICAR	0.0010	**
5	A, pACC/ACC	NT	CC	0.5689	-
5	A, pACC/ACC	NT	CC + AICAR	0.2597	-
5	B	NT	AICAR	0.0264	*
5	B	NT	IFN γ /TNF α	0.0008	**
5	B	NT	IFN γ /TNF α + AICAR	0.0672	-
5	B	NT	CC	0.1400	-
5	B	NT	CC + AICAR	0.1231	-
5	B	NT	CC + IFN γ /TNF α	0.0168	*
5	B	NT	CC + IFN γ /TNF α + AICAR	0.0331	*
5	B	IFN γ /TNF α	IFN γ /TNF α + AICAR	<0.0001	-
5	B	IFN γ /TNF α	CC + IFN γ /TNF α	0.1689	-
5	B	IFN γ /TNF α	CC + IFN γ /TNF α + AICAR	0.0940	-
5	C	NT	AICAR	<0.0001	**
5	C	NT	IFN γ /TNF α	<0.0001	**
5	C	NT	IFN γ /TNF α + AICAR	0.3061	-
5	C	NT	CC	<0.0001	**
5	C	NT	CC + AICAR	<0.0001	**
5	C	NT	CC + IFN γ /TNF α	<0.0001	**
5	C	NT	CC + IFN γ /TNF α + AICAR	<0.0001	**
5	C	IFN γ /TNF α	IFN γ /TNF α + AICAR	<0.0001	-
5	C	IFN γ /TNF α	CC + IFN γ /TNF α	0.7305	-
5	C	IFN γ /TNF α	CC + IFN γ /TNF α + AICAR	<0.0001	-
5	D	NT	AICAR	0.2850	-
5	D	NT	IFN γ /TNF α	<0.0001	**
5	D	NT	IFN γ /TNF α + AICAR	0.0032	**
5	D	NT	CC	0.3247	-
5	D	NT	CC + AICAR	0.4981	-
5	D	NT	CC + IFN γ /TNF α	<0.0001	**
5	D	NT	CC + IFN γ /TNF α + AICAR	0.0002	**
5	D	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0202	†
5	D	IFN γ /TNF α	CC + IFN γ /TNF α	0.9443	-
5	D	IFN γ /TNF α	CC + IFN γ /TNF α + AICAR	0.1561	-
5	E, pS6K/S6K	NT	AICAR	0.1220	-

5	E, pS6K/S6K	NT	IFN γ /TNF α	<0.0001	**
5	E, pS6K/S6K	NT	IFN γ /TNF α + AICAR	0.8872	-
5	E, pS6K/S6K	NT	CC	0.0073	**
5	E, pS6K/S6K	NT	CC + AICAR	<0.0001	**
5	E, pS6K/S6K	NT	CC + IFN γ /TNF α	<0.0001	**
5	E, pS6K/S6K	NT	CC + IFN γ /TNF α + AICAR	<0.0001	**
5	E, pS6K/S6K	IFN γ /TNF α	IFN γ /TNF α + AICAR	<0.0001	-
5	E, pS6K/S6K	IFN γ /TNF α	CC + IFN γ /TNF α	0.9411	-
5	E, pS6K/S6K	IFN γ /TNF α	CC + IFN γ /TNF α + AICAR	0.9537	-
5	E, pS6/S6	NT	AICAR	0.1713	-
5	E, pS6/S6	NT	IFN γ /TNF α	0.0065	**
5	E, pS6/S6	NT	IFN γ /TNF α + AICAR	0.8046	-
5	E, pS6/S6	NT	CC	0.4632	-
5	E, pS6/S6	NT	CC + AICAR	0.2567	-
5	E, pS6/S6	NT	CC + IFN γ /TNF α	0.0067	**
5	E, pS6/S6	NT	CC + IFN γ /TNF α + AICAR	0.0064	**
5	E, pS6/S6	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0038	-
5	E, pS6/S6	IFN γ /TNF α	CC + IFN γ /TNF α	0.9881	-
5	E, pS6/S6	IFN γ /TNF α	CC + IFN γ /TNF α + AICAR	0.9945	-
5	F	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0103	†
5	F	IFN γ /TNF α	CC + IFN γ /TNF α	0.6912	-
5	F	IFN γ /TNF α	CC + IFN γ /TNF α + AICAR	0.4240	-

Abbreviations: NT, non-treated. CC, Compound C

Appendix Table S7. Figure 6 Significance p-values

Figure	Panel	Control	Treatment	p-value	Symbol
6	A	DMSO	A-769662	0.1967	-
6	A	DMSO	IFN γ /TNF α + DMSO	0.0029	**
6	A	DMSO	IFN γ /TNF α + A-769662	0.6624	-
6	A	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662	0.0016	-
6	B	DMSO	A-769662	0.0011	**
6	B	DMSO	IFN γ /TNF α + DMSO	<0.0001	**
6	B	DMSO	IFN γ /TNF α + A-769662	0.1628	-
6	B	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662	<0.0001	-
6	C	DMSO	A-769662	0.0815	-
6	C	DMSO	IFN γ /TNF α + DMSO	0.0031	**
6	C	DMSO	IFN γ /TNF α + A-769662	>0.9999	-
6	C	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662	0.0031	-
6	D, pS6K/S6K	DMSO	A-769662	0.9780	-
6	D, pS6K/S6K	DMSO	IFN γ /TNF α + DMSO	0.0060	**
6	D, pS6K/S6K	DMSO	IFN γ /TNF α + A-769662	0.0501	-
6	D, pS6K/S6K	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662	0.0003	-
6	D, pS6/S6	DMSO	A-769662	0.5221	-
6	D, pS6/S6	DMSO	IFN γ /TNF α + DMSO	0.0011	**
6	D, pS6/S6	DMSO	IFN γ /TNF α + A-769662	0.0650	-
6	D, pS6/S6	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662	0.0221	-
6	E	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662	0.0002	††
6	F	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662	0.0001	††
6	G	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662	<0.0001	††

Appendix Table S8. Figure 7 Significance p-values

Figure	Panel	Control	Treatment	p-value	Symbol
7	A	DMSO	A-769662 25 μ M	0.7863	-
7	A	DMSO	A-769662 50 μ M	0.4685	-
7	A	DMSO	IFN γ /TNF α + DMSO	<0.0001	**
7	A	DMSO	IFN γ /TNF α + A-769662 25 μ M	0.0004	**
7	A	DMSO	IFN γ /TNF α + A-769662 50 μ M	0.0002	**
7	A	DMSO	IFN γ /TNF α + AICAR 125 μ M + DMSO	0.0002	**
7	A	DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 25 μ M	0.0010	**
7	A	DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 50 μ M	0.0034	**
7	A	DMSO	IFN γ /TNF α + AICAR 250 μ M + DMSO	0.0006	**
7	A	DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 25 μ M	0.0647	-
7	A	DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 50 μ M	0.8389	-
7	A	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662 25 μ M	0.2053	-
7	A	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662 50 μ M	0.3064	-
7	A	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + DMSO	0.3386	-
7	A	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 25 μ M	0.1028	-
7	A	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 50 μ M	0.0382	†
7	A	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + DMSO	0.1491	-
7	A	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 25 μ M	0.0018	-
7	A	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 50 μ M	<0.0001	-
7	B	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662 25 μ M	0.4926	-
7	B	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662 50 μ M	0.2623	-
7	B	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + DMSO	0.0797	-

7	B	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 25 μ M	0.6749	-
7	B	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 50 μ M	0.0025	++
7	B	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + DMSO	<0.0001	++
7	B	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 25 μ M	<0.0001	++
7	B	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 50 μ M	<0.0001	++
7	C, pS6K/S6K	DMSO	A-769662 25 μ M	0.0325	*
7	C, pS6K/S6K	DMSO	A-769662 50 μ M	0.0661	-
7	C, pS6K/S6K	DMSO	IFN γ /TNF α + DMSO	<0.0001	**
7	C, pS6K/S6K	DMSO	IFN γ /TNF α + A-769662 25 μ M	<0.0001	**
7	C, pS6K/S6K	DMSO	IFN γ /TNF α + A-769662 50 μ M	<0.0001	**
7	C, pS6K/S6K	DMSO	IFN γ /TNF α + AICAR 125 μ M + DMSO	<0.0001	**
7	C, pS6K/S6K	DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 25 μ M	<0.0001	**
7	C, pS6K/S6K	DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 50 μ M	<0.0001	**
7	C, pS6K/S6K	DMSO	IFN γ /TNF α + AICAR 250 μ M + DMSO	<0.0001	**
7	C, pS6K/S6K	DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 25 μ M	0.0069	**
7	C, pS6K/S6K	DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 50 μ M	0.0809	-
7	C, pS6K/S6K	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662 25 μ M	0.7856	-
7	C, pS6K/S6K	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662 50 μ M	0.7596	-
7	C, pS6K/S6K	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + DMSO	0.7596	-
7	C, pS6K/S6K	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 25 μ M	0.8918	-
7	C, pS6K/S6K	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 50 μ M	0.0039	++
7	C, pS6K/S6K	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + DMSO	0.0350	†

7	C, pS6K/S6K	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 25 μ M	<0.0001	++
7	C, pS6K/S6K	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 50 μ M	<0.0001	-
7	C, pS6/S6	DMSO	A-769662 25 μ M	0.7896	-
7	C, pS6/S6	DMSO	A-769662 50 μ M	0.6209	-
7	C, pS6/S6	DMSO	IFN γ /TNF α + DMSO	<0.0001	**
7	C, pS6/S6	DMSO	IFN γ /TNF α + A-769662 25 μ M	<0.0001	**
7	C, pS6/S6	DMSO	IFN γ /TNF α + A-769662 50 μ M	<0.0001	**
7	C, pS6/S6	DMSO	IFN γ /TNF α + AICAR 125 μ M + DMSO	<0.0001	**
7	C, pS6/S6	DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 25 μ M	<0.0001	**
7	C, pS6/S6	DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 50 μ M	0.0004	**
7	C, pS6/S6	DMSO	IFN γ /TNF α + AICAR 250 μ M + DMSO	<0.0001	**
7	C, pS6/S6	DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 25 μ M	0.0017	**
7	C, pS6/S6	DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 50 μ M	0.0994	-
7	C, pS6/S6	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662 25 μ M	0.7981	-
7	C, pS6/S6	IFN γ /TNF α + DMSO	IFN γ /TNF α + A-769662 50 μ M	0.9773	-
7	C, pS6/S6	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + DMSO	0.9094	-
7	C, pS6/S6	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 25 μ M	0.4134	-
7	C, pS6/S6	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 125 μ M + A-769662 50 μ M	0.0012	++
7	C, pS6/S6	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + DMSO	0.3984	-
7	C, pS6/S6	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 25 μ M	0.0021	++
7	C, pS6/S6	IFN γ /TNF α + DMSO	IFN γ /TNF α + AICAR 250 μ M + A-769662 50 μ M	<0.0001	-

Appendix Table S9. Figure 8 Significance p-values

Figure	Panel	Control	Treatment	p-value	Symbol
8	C	Saline	C26	<0.0001	**
8	C	Saline	C26 + AICAR	<0.0001	**
8	C	Saline	C26 + MET	<0.0001	**
8	C	C26	C26 + AICAR	<0.0001	††
8	C	C26	C26 + MET	0.0194	†
8	D	Saline	C26	0.0043	**
8	D	Saline	C26 + AICAR	0.0956	-
8	D	Saline	C26 + MET	0.0081	**
8	D	C26	C26 + AICAR	0.0743	-
8	D	C26	C26 + MET	0.6698	-
8	E	Saline	C26	0.0190	*
8	E	Saline	C26 + AICAR	0.0690	-
8	E	Saline	C26 + MET	0.0268	*
8	E	C26	C26 + AICAR	0.4305	-
8	E	C26	C26 + MET	0.8296	-

Abbreviations: MET, metformin.

Appendix Table S10. Figure 9 Significance p-values

Figure	Panel	Control	Treatment	p-value	Symbol
9	A	PF	LPS	<0.0001	**
9	A	PF	LPS + AICAR	0.1205	-
9	A	PF	LPS + MET	<0.0001	**
9	A	LPS	LPS + AICAR	<0.0001	-
9	A	LPS	LPS + MET	0.9987	-
9	B	PF	LPS	0.0194	*
9	B	PF	LPS + AICAR	0.5364	-
9	B	PF	LPS + MET	0.0233	*
9	B	LPS	LPS + AICAR	0.0670	-
9	B	LPS	LPS + MET	0.9297	-
9	C	PF	LPS	0.0026	**
9	C	PF	LPS + AICAR	0.1666	-
9	C	PF	LPS + MET	0.0040	**
9	C	LPS	LPS + AICAR	0.0506	-
9	C	LPS	LPS + MET	0.8428	-

Abbreviations: PF, pair-fed controls. MET, metformin.

Appendix Table S11. Figure EV3 Significance p-values

Figure	Panel	Control	Treatment	p-value	Symbol
EV3	A	C26	C26 + AICAR	0.0113	†
EV3	A	C26	C26 + MET	0.0180	†
EV3	B	Saline	C26	0.0078	**
EV3	B	Saline	C26 + AICAR	0.7341	-
EV3	B	Saline	C26 + MET	0.7652	-
EV3	B	C26	C26 + AICAR	0.0047	-
EV3	B	C26	C26 + MET	0.0050	-

Abbreviations: MET, metformin.

Appendix Table S12. Figure EV4 Significance p-values

Figure	Panel	Control	Treatment	p-value	Symbol
EV4	B	Day 14, Saline	Day 14, C26	0.0107	*
EV4	B	Day 14, Saline	Day 14, C26 + AICAR	0.0049	**
EV4	B	Day 21, Saline	Day 21, C26	<0.0001	**
EV4	B	Day 21, Saline	Day 21, C26 + AICAR	0.0004	**
EV4	B	Day 14, Saline	Day 21, Saline	0.9795	-
EV4	B	Day 14, C26	Day 21, C26	0.0001	**
EV4	B	Day 14, C26 + AICAR	Day 21, C26 + AICAR	0.0889	NS
EV4	C, Atrogin1	Saline	C26	0.0003	**
EV4	C, Atrogin1	Saline	C26 + AICAR	0.3442	-
EV4	C, Atrogin1	C26	C26 + AICAR	0.0012	-
EV4	C, MuRF1	Saline	C26	0.0074	**
EV4	C, MuRF1	Saline	C26 + AICAR	0.0173	*
EV4	C, MuRF1	C26	C26 + AICAR	0.6088	-

Abbreviations: NS, not significant

Appendix Table S13. Figure EV5 Significance p-values

Figure	Panel	Control	Treatment	p-value	Symbol
EV5	A	Saline	AICAR	0.6095	-
EV5	A	Saline	IFN γ /TNF α	0.0010	**
EV5	A	Saline	IFN γ /TNF α + AICAR	0.0010	**
EV5	A	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.9099	-
EV5	B	Saline	AICAR	0.4364	-
EV5	B	Saline	IFN γ /TNF α	0.0244	*
EV5	B	Saline	IFN γ /TNF α + AICAR	0.7582	NS
EV5	B	IFN γ /TNF α	IFN γ /TNF α + AICAR	0.0554	-

Abbreviations: NS, not significant

Appendix Table S14. Table 1 Significance p-values

Table	Variable	Control	Treatment	p-value	Symbol
1	Body Weight Change	Saline	C26	<0.0001	**
1	Body Weight Change	Saline	C26 + AICAR	<0.0001	**
1	Body Weight Change	Saline	C26 + MET	<0.0001	**
1	Body Weight Change	C26	C26 + AICAR	0.0004	††
1	Body Weight Change	C26	C26 + MET	0.2284	-
1	Tibialis Anterior	Saline	C26	<0.0001	**
1	Tibialis Anterior	Saline	C26 + AICAR	0.0160	*
1	Tibialis Anterior	Saline	C26 + MET	<0.0001	**
1	Tibialis Anterior	C26	C26 + AICAR	0.0341	†
1	Tibialis Anterior	C26	C26 + MET	0.7884	-
1	Gastrocnemius	Saline	C26	<0.0001	**
1	Gastrocnemius	Saline	C26 + AICAR	0.0006	**
1	Gastrocnemius	Saline	C26 + MET	<0.0001	**
1	Gastrocnemius	C26	C26 + AICAR	0.0107	†
1	Gastrocnemius	C26	C26 + MET	0.4784	-
1	Fat Pad	Saline	C26	<0.0001	**
1	Fat Pad	Saline	C26 + AICAR	<0.0001	**
1	Fat Pad	Saline	C26 + MET	<0.0001	**
1	Fat Pad	C26	C26 + AICAR	0.6562	-
1	Fat Pad	C26	C26 + MET	0.9207	-
1	Tumor	C26	C26 + AICAR	0.8997	-
1	Tumor	C26	C26 + MET	0.8605	-
1	IL-6	Saline	C26	0.0019	**
1	IL-6	Saline	C26 + AICAR	0.0105	*
1	IL-6	Saline	C26 + MET	0.1123	-
1	IL-6	C26	C26 + AICAR	0.3767	-
1	IL-6	C26	C26 + MET	0.0455	†

Abbreviations: MET, metformin.

Appendix Table S15. Table 2 Significance p-values

Table	Variable	Control	Treatment	p-value	Symbol
2	Body Weight Change	PF	Veh.	<0.0001	**
2	Body Weight Change	PF	LPS	0.4611	-
2	Body Weight Change	PF	LPS + AICAR	0.0221	*
2	Body Weight Change	PF	LPS + MET	0.1424	-
2	Body Weight Change	LPS	LPS + AICAR	0.0032	-
2	Body Weight Change	LPS	LPS + MET	0.4569	-
2	Tibialis Anterior	PF	Veh.	0.6981	-
2	Tibialis Anterior	PF	LPS	0.0080	**
2	Tibialis Anterior	PF	LPS + AICAR	0.5768	-
2	Tibialis Anterior	PF	LPS + MET	0.0268	*
2	Tibialis Anterior	LPS	LPS + AICAR	0.0316	-
2	Tibialis Anterior	LPS	LPS + MET	0.6255	-
2	Gastrocnemius	PF	Veh.	0.0740	-
2	Gastrocnemius	PF	LPS	0.0330	*
2	Gastrocnemius	PF	LPS + AICAR	0.8263	-
2	Gastrocnemius	PF	LPS + MET	0.0368	*
2	Gastrocnemius	LPS	LPS + AICAR	0.0539	-
2	Gastrocnemius	LPS	LPS + MET	0.9629	-
2	Fat Pad	PF	Veh.	0.9299	-
2	Fat Pad	PF	LPS	0.6192	-
2	Fat Pad	PF	LPS + AICAR	0.9013	-
2	Fat Pad	PF	LPS + MET	0.5519	-
2	Fat Pad	LPS	LPS + AICAR	0.5351	-
2	Fat Pad	LPS	LPS + MET	0.9215	-

Abbreviations: PF, pair-fed controls. Veh., Vehicle. MET, metformin.