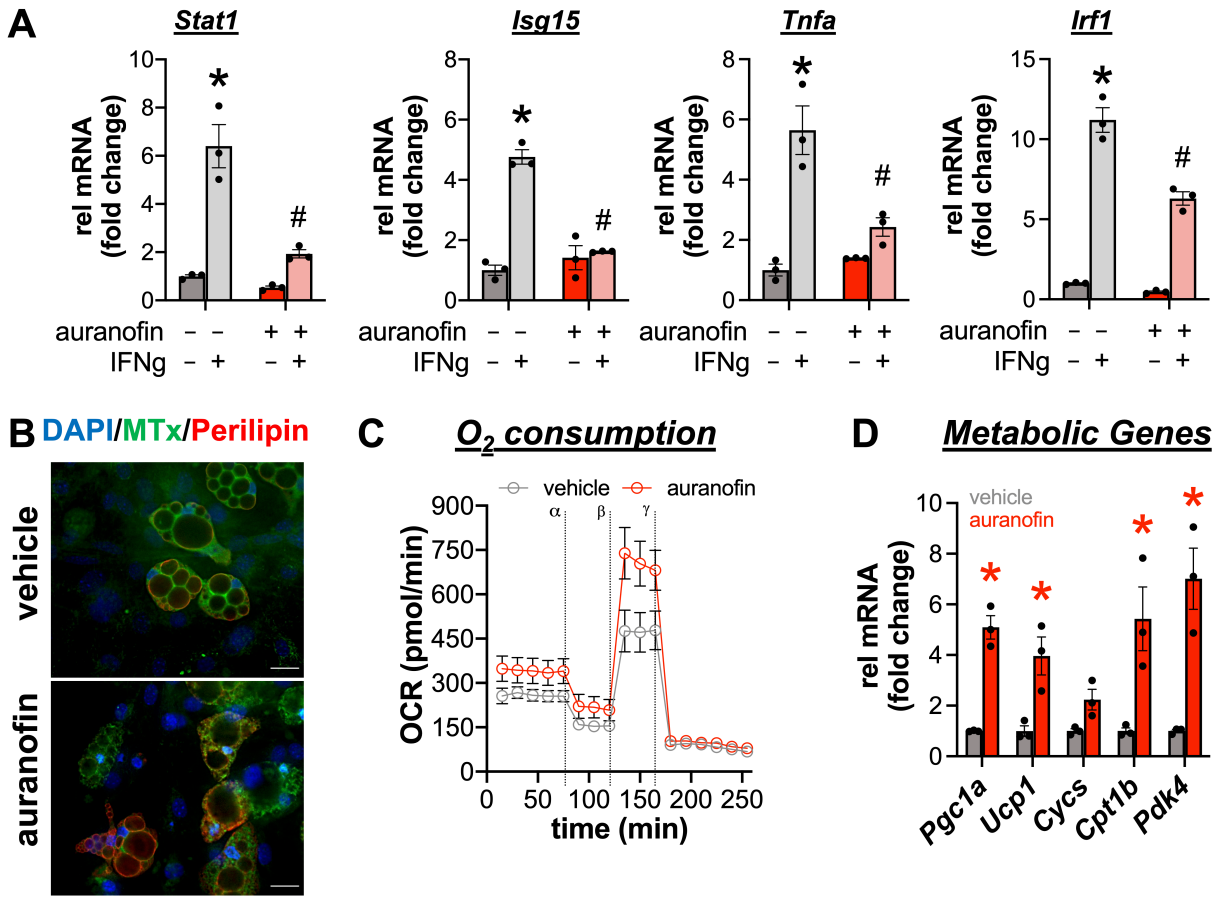
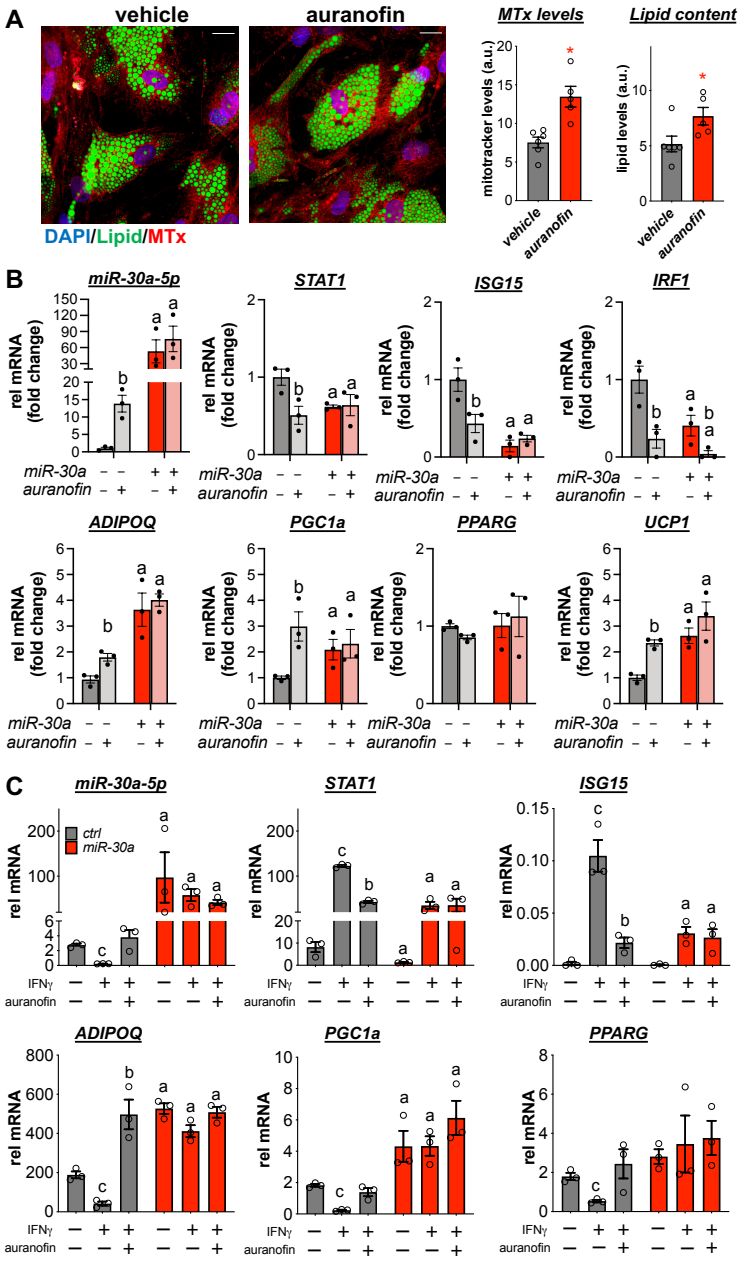
Supplemental Figures and Legends

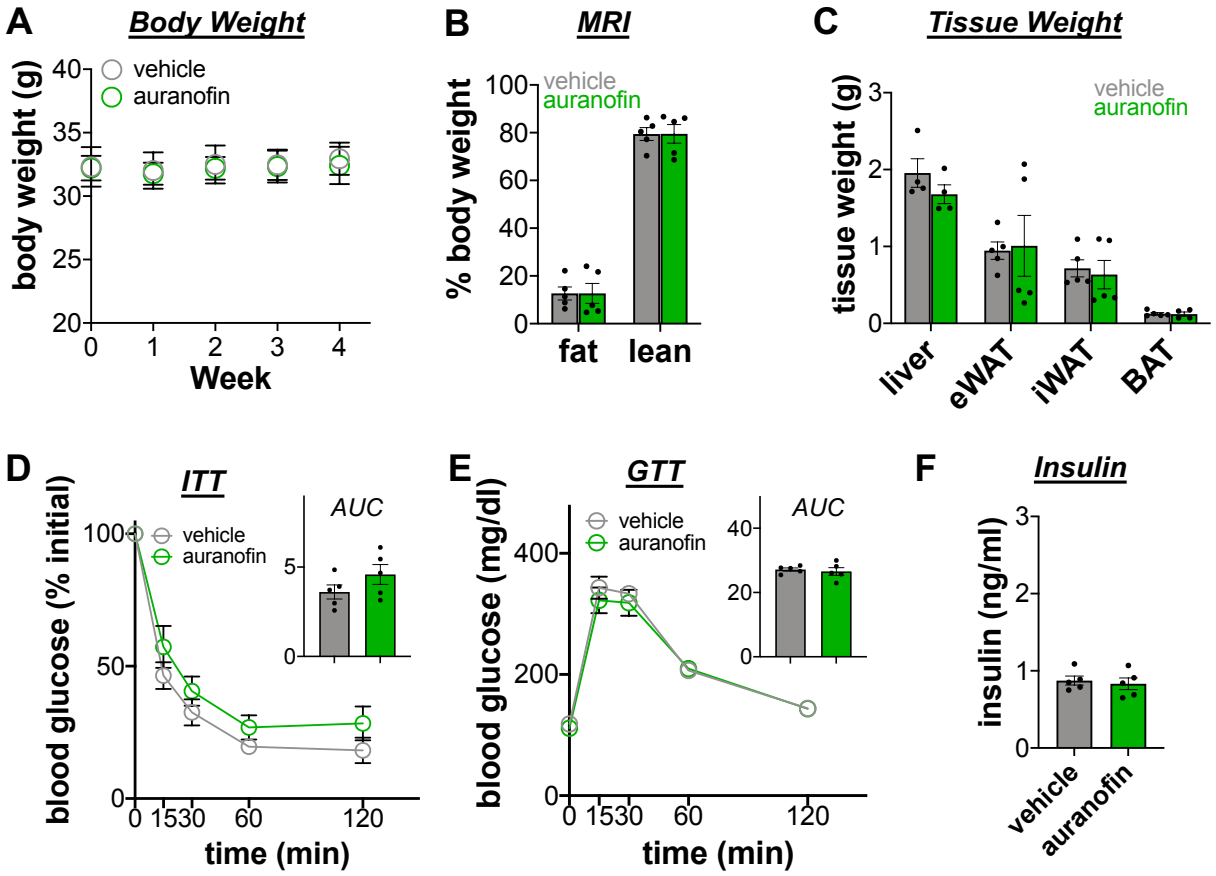
Supplemental Figure S1. Anti-inflammatory and metabolic effects of auranofin in mouse adipocytes, Related to Figure 1. **(A)** WAT stromal vascular cells (SVF) were differentiated into adipocytes and then exposed to auranofin (1000 nM) or vehicle (DMSO) +/- IFNg (100 ng/ml; hatched bars). Relative mRNA expression of inflammatory genes. **(B)** Immunofluorescence (DAPI – blue, perilipin – red, MitoTracker – green) images of differentiated adipocytes from WAT SVF in the presence of auranofin (100 nM) or DMSO for 24 h. Scale bar, 20 μm **(C)** Respiration (as oxygen consumption rate, OCR) in differentiated mouse adipocytes measured during the Seahorse XF Mitochondrial Stress kit (a = oligomycin, b = FCCP, g = rotenone/antimycin A). **(D)** Relative mRNA expression of metabolic genes in differentiated adipocytes exposed to auranofin (1000 nM; red) or vehicle (DMSO; gray).
All data are represented as mean ± SEM.
*p<0.05 vs DMSO vehicle, #p<0.05 vs IFNg alone by 2-way ANOVA with Tukey's multiple comparison's test: **(A)**; **(D)**



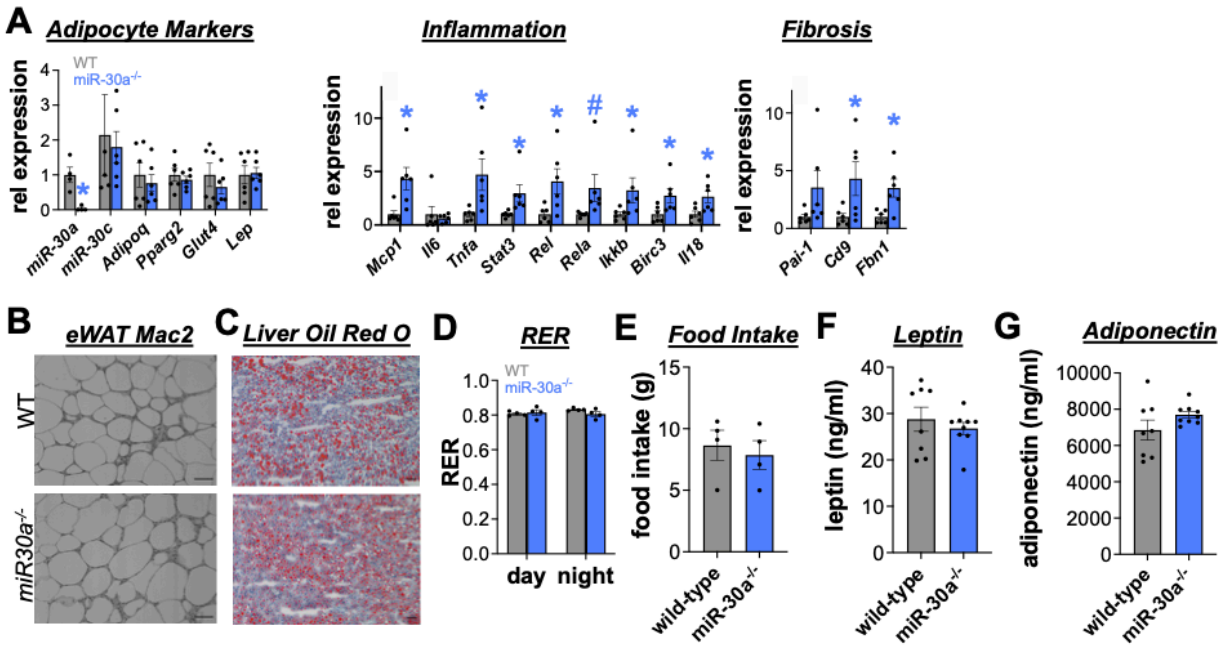
Supplemental Figure S2. Auranofin and *miR-30a* exhibit similar activities in human adipocytes, Related to Figure 1. (A) Immunofluorescence (DAPI – blue, MitoTracker – red, LipidTox – green) images of differentiated human adipocytes in the presence of auranofin (100 nM) or DMSO for 24 h. Scale bar, 20 µm. Quantification performed on 4-5 fields/treatment and at least 10 cells/field. **(B)** Human adipocytes transfected with control (gray) or *miR-30a* mimics (red) 48 h followed by auranofin (100 nM) or vehicle (DMSO) treatments for 24 h. Relative mRNA expression of inflammatory and metabolic genes. **(C)** After 48 h transfection with control or *miR-30a* mimics, cells were pretreated for 6 h with auranofin (100 nM) followed by IFNg (100 ng/ml) exposure overnight. Relative mRNA expression of inflammatory and metabolic genes. All data are represented as mean ± SEM.
*p<0.05 vs DMSO by unpaired student t-test: **(A)**
[a]p<0.05 vs [a]control mimic, [b]auranofin, [c]IFNg by 2-way ANOVA with Tukey's multiple comparison's test: **(B)**; **(C)**



Supplemental Figure S3. The metabolic effects of auranofin require obesity, Related to Figure 2. Mice fed a normal chow diet (NC) were i.p. injected with auranofin (1 mg/kg; green) or vehicle (gray) for 4 weeks starting at 18 weeks of age (n=5/group). **(A)** Body weight during treatment with **(B)** final body composition (% body mass). **(C)** Tissue weights (g). **(D)** Insulin (ITT) and **(E)** glucose (GTT) tolerance tests, with corresponding area under the curve (AUC) measurements (x10^4 or x10^5, respectively). **(F)** Overnight fasting serum insulin (ng/ml).
Data are represented as mean ± SEM.
*p<0.05, #p<0.10 by unpaired t-test: **(C)**; AUC in **(D)**, **(E)**, **(F)**
*p<0.05, #p<0.10 by 2-way ANOVA with Tukey's multiple comparisons test: **(A)**; **(B)**; **(D)**; **(E)**



Supplemental Figure S4. HFD affects energy balance in miR-30a$^{-/-}$ and wild-type littermates, Related to Figure 4. Six week old male *miR-30a*$^{-/-}$ and wild-type (WT) littermates were exposed to HFD for 16 weeks. **(A)** Relative mRNA expression of adipocyte marker, inflammatory, and fibrosis genes from eWAT (n=4-6/group). **(B)** eWAT Mac2 IHC and **(C)** liver Oil-Red-O; scale bar = 50 μm. Mice were individually housed and monitored in CLAMS home cages for 6 days (n=5/group). **(D)** Averaged RER measurements during dark and light periods and **(E)** cumulative food intake. **(F)** Fed serum leptin (ng/ml) and **(G)** adiponectin (ng/ml) for n=6-8/group.
All data are represented as mean ± SEM.
*p<0.05, unpaired t-test: **(A)**; **(E)**; **(F)**; **(G)**
#p<0.10 by ANCOVA with lean mass as a co-variate **(D)**



Supplemental Figure S5. Leptin deficient mice are resistant to the insulin sensitizing effects of auranofin, Related to Figure 6. Male ob/ob mice were i.p. injected with auranofin (orange) or vehicle (gray) for 4 weeks starting at 18 weeks of age (n=3-4/group). **(A)** Body weight during treatment with **(B)** final body composition (% body mass). **(C)** Tissue weights (g). **(D)** eWAT H&E; scale bar = 50 μm. **(E)** Insulin (ITT) and **(F)** glucose (GTT) tolerance tests, with corresponding area under the curve (AUC) measurements ($x10^4$ or $x10^5$, respectively). **(G)** Overnight fasting serum insulin (ng/ml). **(H)** Liver H&E; scale bar = 50 μm. **(I)** Relative mRNA expression of inflammatory, fibrosis, and metabolism genes from eWAT of ob/ob mice treated with auranofin or vehicle (n=3/group). **(J)** Glycerol (mM/μg protein) release into the media two hours after stimulation (n=4-5/group).
Data are represented as mean ± SEM.
*p<0.05, #p<0.10 by unpaired t-test: **(C)**; AUC in **(E)**, **(G)**; **(I)**
*p<0.05, #p<0.10 by 2-way ANOVA with Tukey's multiple comparisons test: **(A)**; **(B)**; **(E)**; **(F)**; **(J)**