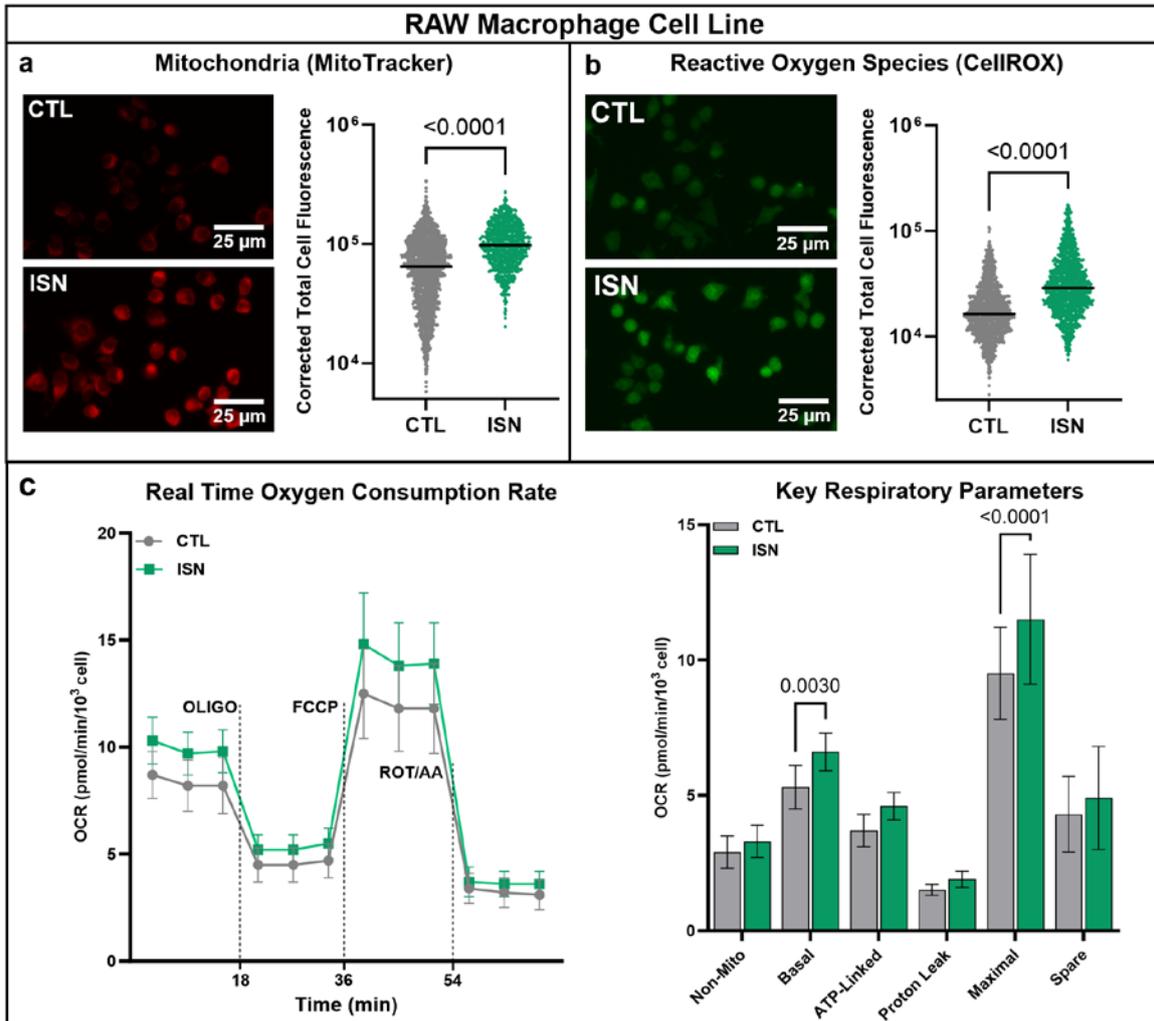


Supplements



**Supplemental Figure S1.** Fluorescence imaging and metabolic analysis data from experimental repeats in RAW 264.7 macrophage cell line. Mitochondrial fluorescence via MitoTracker corrected total cell fluorescence significantly increased with 10 ng/mL of irisin (ISN) versus untreated controls (CTL) (a). Reactive oxygen species concentrations via CellROX corrected total cell fluorescence significantly increased with irisin treatment (b). Real-time oxygen consumption rates (OCR) elevated with irisin treatment, leading to increased basal and maximal respiration (c). *p*-values via unpaired, two-tailed Student's *t*-test (a,b) and 2-way ANOVA (c), with significant values ( $p < 0.05$ ) are displayed on graph.

**Supplemental Table S1.** Summary data of technical replicate number (n), mean, standard deviation (StDev), and *p*-value for experimental replicates in primary and RAW cell line osteoclasts (OCL).

Metric	Experiment	Group	n	Mean	StDev	P-value
MitoTracker CTCF (Arbitrary Units)	Primary OCL 1	CTL	734	142063	82220	<0.0001
		ISN	509	214165	140989	
	Primary OCL 2	CTL	1341	67641	57318	<0.0001
		ISN	923	81922	71824	
	RAW OCL	CTL	1886	70645	43974	<0.0001
		ISN	859	104107	42427	
CellROX CTCF (Arbitrary Units)	Primary OCL 1	CTL	657	40979	36034	<0.0001
		ISN	758	76617	58977	
	Primary OCL 2	CTL	1200	45144	35614	0.0005
		ISN	626	51034	32040	
	RAW OCL	CTL	1347	20288	13350	<0.0001
		ISN	1231	36735	26948	
Non-Mito OCR (pmol/min/10 <sup>3</sup> cells)	Primary OCL 1	CTL	23	1.5	0.5	0.9842
		ISN	23	1.7	0.5	
	Primary OCL 2	CTL	16	2.4	0.3	0.9999
		ISN	16	2.5	0.4	
	RAW OCL	CTL	20	2.9	0.6	0.8585
		ISN	22	3.3	0.6	
Basal OCR (pmol/min/10 <sup>3</sup> cells)	Primary OCL 1	CTL	23	3.1	0.9	0.8931
		ISN	23	3.4	0.7	
	Primary OCL 2	CTL	16	4.6	0.8	0.9565
		ISN	16	4.9	0.5	
	RAW OCL	CTL	20	5.3	0.8	0.003
		ISN	22	6.6	0.7	
ATP-Linked OCR (pmol/min/10 <sup>3</sup> cells)	Primary OCL 1	CTL	23	1.9	0.7	0.9842
		ISN	23	2.1	0.5	
	Primary OCL 2	CTL	16	3.1	0.6	0.9945
		ISN	16	3.3	0.3	
	RAW OCL	CTL	20	3.7	0.6	0.0877
		ISN	22	4.6	0.5	
Proton Leak OCR (pmol/min/10 <sup>3</sup> cells)	Primary OCL 1	CTL	23	1.2	0.2	0.9997
		ISN	23	1.3	0.3	
	Primary OCL 2	CTL	16	1.5	0.3	0.9999
		ISN	16	1.6	0.3	
	RAW OCL	CTL	20	1.5	0.2	0.8585
		ISN	22	1.9	0.3	
Maximal OCR (pmol/min/10 <sup>3</sup> cells)	Primary OCL 1	CTL	23	8.5	1.6	<0.0001
		ISN	23	10.9	1.7	
	Primary OCL 2	CTL	16	10.2	1.8	0.0064
		ISN	16	11.4	1.8	
	RAW OCL	CTL	20	9.5	1.7	<0.0001
		ISN	22	11.5	2.4	
Spare OCR (pmol/min/10 <sup>3</sup> cells)	Primary OCL 1	CTL	23	5.4	1.3	<0.0001
		ISN	23	7.5	1.5	
	Primary OCL 2	CTL	16	5.6	1.3	0.0785
		ISN	16	6.5	1.6	
	RAW OCL	CTL	20	4.3	1.4	0.4837
		ISN	22	4.9	1.9	