Involution	Harvest Day Post-Partum	Days Post Complete Weaning
AI	28	21
AI	56	49
AI	120	113
GI	56	25
GI	120	89

Supplementary File S1. Experimental Timeline of Harvest versus Post Complete Weaning Days in AI & GI Groups

a.

Time Comparison	Ingenuity Canonical Pathways	-log(B-H p-val	Ratio	z-score
d28 AI vs d56 GI	Processing of Capped Intron-Containing Pre-mRNA	26.9	0.389	9.099
	Major pathway of rRNA processing in the nucleolus and cytosol	23.6	0.397	7.672
	RNA Polymerase II Transcription	13.1	0.38	6.682
	Synthesis of DNA	7.59	0.336	6.008
	Assembly of RNA Polymerase II Complex	7.48	0.471	3.545
	Neutrophil degranulation	7.23	0.22	6.139
	mRNA Capping	5.85	0.533	3.5
	RNA polymerase II transcribes snRNA genes	5.76	0.349	3.657
	DNA Replication Pre-Initiation	5.51	0.317	5.745
	rRNA modification in the nucleus and cytosol	4.13	0.333	4.243
	mRNA 3 Prime End Processing Signaling Pathway	3.8	0.284	3.128
	Estrogen Receptor Signaling	2.47	0.182	1.871
	Processing of Capped Intronless Pre-mRNA	1.42	0.31	2.121
	RNA Polymerase III Transcription	1.3	0.268	3.317
	DNA Double Strand Break Response	0.961	0.22	1.387
	DNA Damage Bypass	0.919	0.229	1.897
	Extra-nuclear estrogen signaling	0.25	0.147	1.508
	Estrogen Biosynthesis	0.237	0.152	-1
	rRNA processing	0	0.0938	N/A
	Cellular response to hypoxia	10.6	0.461	4.902
	Insulin Secretion Signaling Pathway	4.34	0.222	1.069
	Mitochondrial protein import	4.06	0.338	2.4
	Cellular response to heat stress	3.89	0.287	2.858
	Oxidative Phosphorylation	3.42	0.271	1.8
	Cristae formation	3.04	0.394	3.051
	Complex I biogenesis	2.82	0.294	2.524
	Cellular response to mitochondrial stress	2.67	0.667	1.633
	Mitochondrial translation	2.62	0.258	3.411
	Insulin Receptor Signaling	2.39	0.233	0.6
	Mitochondrial protein degradation	2.22	0.245	0.816
	Translocation of SLC2A4 (GLUT4) to the plasma membrane	2.11	0.264	1.606
	NRF2-mediated Oxidative Stress Response	1.99	0.189	2.668
	Adipogenesis pathway	1.98	0.217	-0.928
	Complex IV assembly	1.95	0.292	2.887
	Detoxification of Reactive Oxygen Species	1.59	0.297	3.317
	Respiratory electron transport	1.53	0.227	2.236
	Transcriptional regulation of white adipocyte differentiation	1.43	0.226	0.688
	Glycolysis I	1.42	0.31	-0.816
	Glucose metabolism	1.07	0.207	0.5
	Glycerophospholipid biosynthesis	0.989	0.188	1.043
	Complex III assembly	0.936	0.28	-0.378
	Signaling by Insulin receptor	0.789	0.222	2.53

b.

Time Comparison	Ingenuity Canonical Pathways	-log(B-H p-val	Ratio	z-score
d120 AI vs GI	Oxidative Phosphorylation	5.23	0.134	-3.873
	Mitochondrial Dysfunction	3.99	0.0698	2.041
	Mitochondrial translation	3.03	0.115	-3.317
	Glycolysis I	2.71	0.222	-2.236
	Gluconeogenesis I	2.71	0.222	-2.236
	Glucose metabolism	1.61	0.1	-2.121
	Mitochondrial protein import	1.04	0.0938	-2.449
	Cristae formation	0.844	0.129	-2
	Mitochondrial biogenesis	0.567	0.0781	-2.236

c.

Time Comparison	Ingenuity Canonical Pathways	-log(B-H p-val	Ratio	z-score
Tam vs Placebo	Glycolysis I	4.06	0.379	2.53
	Adipogenesis pathway	2.47	0.145	0.447
	Neutrophil degranulation	1.74	0.0901	-0.926
	Glucose metabolism	1.36	0.138	2.309
	Mitochondrial Dysfunction	0.98	0.0841	-0.853
	Oxidative Phosphorylation	0.968	0.112	2.828
	Glycerophospholipid biosynthesis	0.843	0.102	-1.732
	Complex I biogenesis	0.777	0.118	2.646
	Insulin Receptor Signaling	0.658	0.093	0.577
	Respiratory electron transport	0.648	0.102	3
	Insulin Secretion Signaling Pathway	0.525	0.0753	-2.183

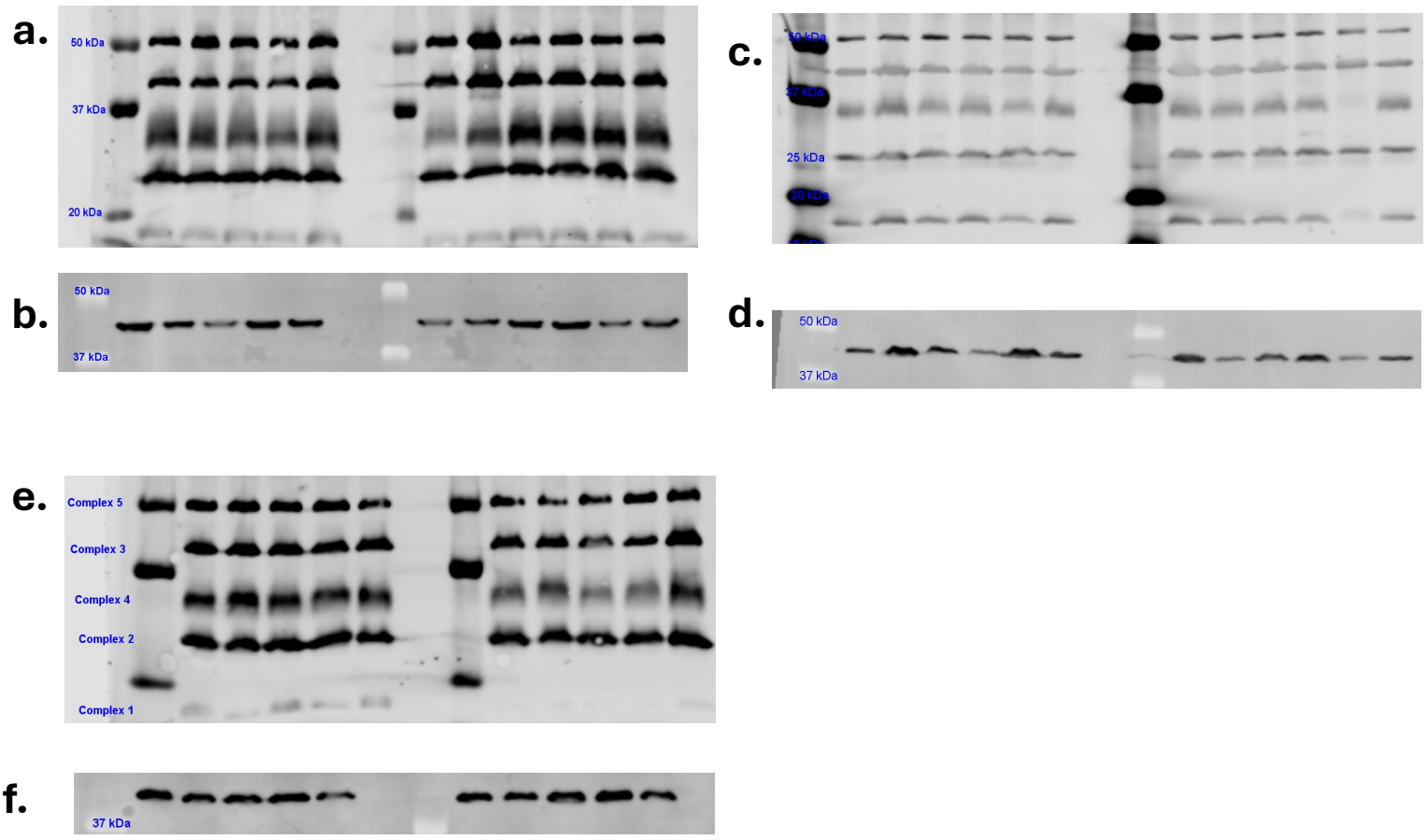
d.

Time Comparison	Ingenuity Canonical Pathways	-log(B-H p-val	Ratio	z-score
PABC ER- vs ER+	Insulin Secretion Signaling Pathway	2	0.154	0.156
	Mitochondrial Dysfunction	1.44	0.133	1.234
	Pyruvate metabolism	1.24	0.204	-0.707
	Fatty acyl-CoA biosynthesis	1.13	0.216	-0.707
	Signaling by Insulin receptor	1.1	0.2	-1.667
	Triglyceride metabolism	1.08	0.211	1.134
	Mitochondrial Division Signaling Pathway	1	0.139	0.209
	Mitochondrial translation	0.981	0.155	-2.324
	Mitochondrial biogenesis	0.981	0.172	0.302
	Integration of energy metabolism	0.94	0.148	-0.5

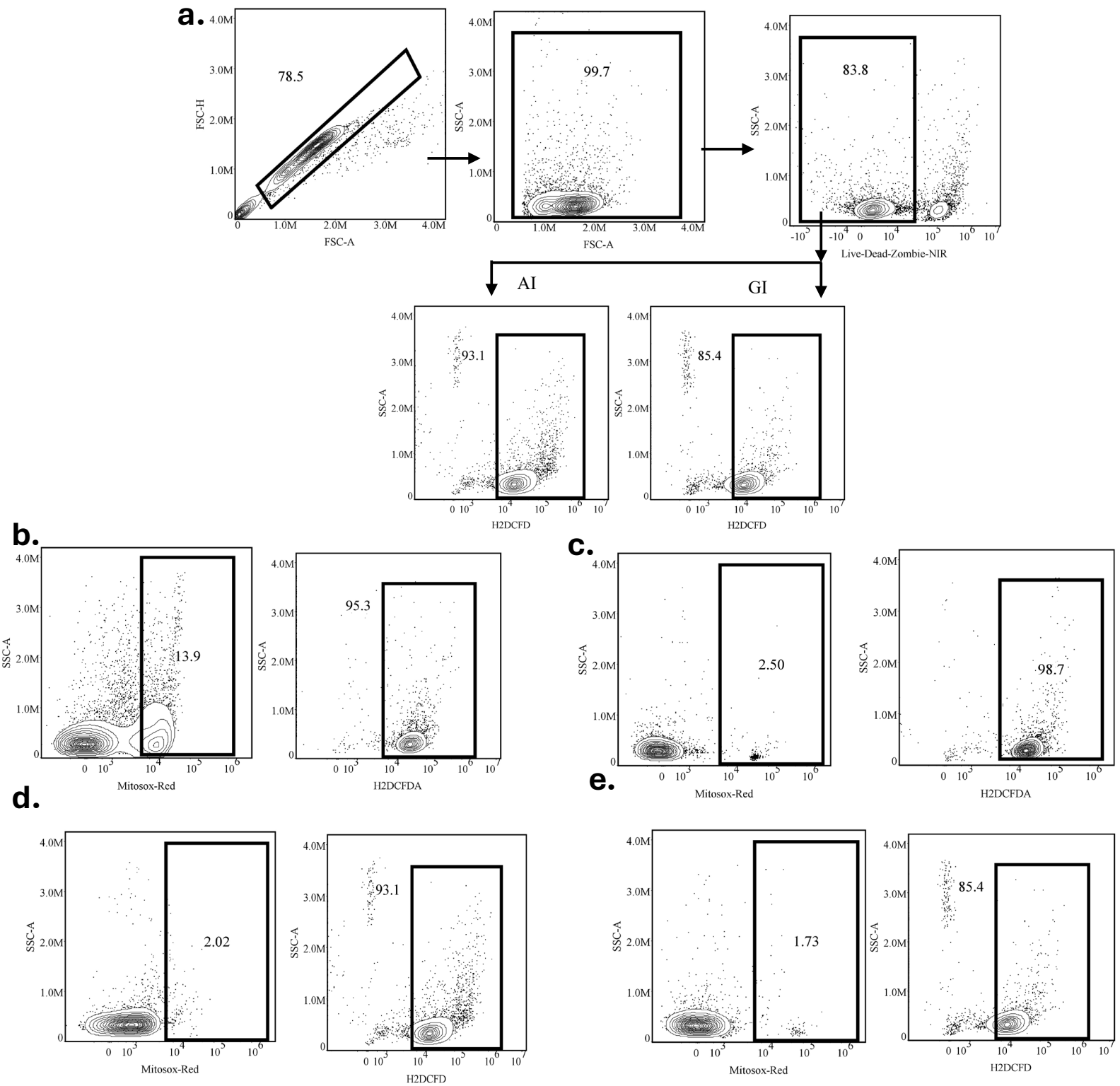
Supplementary File S2. *Ingenuity Pathway Analysis BH/FDR Values* **a**. Pathway comparison day 28 AI and day 56 GI. **b**. Pathway comparison day 120 AI and GI. **c**. Pathway comparison day 28 tamoxifen and AI placebo. **d**. Pathway comparison PABC ER- and PABC ER+.

Gene Name	Forward Sequence	Reverse Sequence
CSN2	TGTGGCCCTTGCTCTTGC	CCTGGAGCACATCCTCTGC
WAP	ATAGAATGCTCCAGCGACCG	TGAAGGGTTATCACTGGCACT
RPL37	AGAAGCAAGATGACGAAGGGAA	CTTGGGTTTCGGCGTTGTTC

Supplementary File S3. qPCR Primer Sequences



Supplementary File S4. *Full Western Blots Analyzed.* **a**. Mitochondrial Complexes day 28 AI vs day 56 GI. **b**. β-Actin day 28 AI vs day 56 GI. **c**. Mitochondrial complexes day 120 AI vs GI. **d**. β-Actin day 120 AI vs GI. **e**. Mitochondrial complexes tamoxifen vs placebo day 28. **f**. β-Actin tamoxifen vs placebo day 28.


a.
78.5
FSC-H
FSC-A
99.7
SSC-A
FSC-A
83.8
SSC-A
Live-Dead-Zombie-NIR
AI
GI
93.1
85.4
SSC-A
H2DCFD
b.
13.9
95.3
SSC-A
Mitosox-Red
H2DCFDA
c.
2.50
98.7
SSC-A
Mitosox-Red
H2DCFDA
d.
2.02
93.1
SSC-A
Mitosox-Red
H2DCFD
e.
1.73
85.4
SSC-A
Mitosox-Red
H2DCFD

Supplementary File S5. *Oxidative Stress Flow Cytometry Raw Data* **a**. Exclusion and viability schematic. **b**. Day 28 AI Mitosox-Red and H2CFDA. **c**. Day 56 GI Mitosox-Red and H2CFDA **d**. Day 120 AI Mitosox-Red and H2CFDA. **e.** Day 120 GI Mitosox-Red and H2CFDA.