

Pathways	Total	Expected	Hits	Raw p	Holm p	FDR	Impact
Aminoacyl-tRNA biosynthesis	69	0.88	11	3.98E-11	3.26E-09	3.26E-09	0.00
Arginine and proline metabolism	44	0.56	5	1.45E-04	1.18E-02	5.96E-03	0.32
Valine, leucine and isoleucine biosynthesis	11	0.14	3	2.67E-04	2.14E-02	7.30E-03	1.00
Alanine, aspartate and glutamate metabolism	24	0.30	3	2.95E-03	2.33E-01	6.05E-02	0.15
Nitrogen metabolism	9	0.11	2	5.21E-03	4.06E-01	8.54E-02	0.00
Valine, leucine and isoleucine degradation	38	0.48	3	1.10E-02	8.47E-01	1.50E-01	0.00
Glutathione metabolism	26	0.33	2	4.14E-02	1.00E+00	4.24E-01	0.01
Galactose metabolism	26	0.33	2	4.14E-02	1.00E+00	4.24E-01	0.04
Glycine, serine and threonine metabolism	31	0.39	2	5.70E-02	1.00E+00	5.08E-01	0.27
D-Glutamine and D-glutamate metabolism	5	0.06	1	6.20E-02	1.00E+00	5.08E-01	0.00
Cyanoamino acid metabolism	6	0.08	1	7.40E-02	1.00E+00	5.51E-01	0.00
Methane metabolism	9	0.11	1	1.09E-01	1.00E+00	7.45E-01	0.00
Selenoamino acid metabolism	15	0.19	1	1.75E-01	1.00E+00	1.00E+00	0.00
Pantothenate and CoA biosynthesis	15	0.19	1	1.75E-01	1.00E+00	1.00E+00	0.00
Glyoxylate and dicarboxylate metabolism	18	0.23	1	2.07E-01	1.00E+00	1.00E+00	0.00
Starch and sucrose metabolism	19	0.24	1	2.17E-01	1.00E+00	1.00E+00	0.04
Citrate cycle (TCA cycle)	20	0.25	1	2.27E-01	1.00E+00	1.00E+00	0.05
Fructose and mannose metabolism	21	0.27	1	2.37E-01	1.00E+00	1.00E+00	0.13
Pyruvate metabolism	23	0.29	1	2.56E-01	1.00E+00	1.00E+00	0.00
Porphyryn and chlorophyll metabolism	27	0.34	1	2.94E-01	1.00E+00	1.00E+00	0.00
Cysteine and methionine metabolism	27	0.34	1	2.94E-01	1.00E+00	1.00E+00	0.09
Glycerophospholipid metabolism	30	0.38	1	3.21E-01	1.00E+00	1.00E+00	0.00
Pyrimidine metabolism	41	0.52	1	4.12E-01	1.00E+00	1.00E+00	0.00
Tyrosine metabolism	44	0.56	1	4.35E-01	1.00E+00	1.00E+00	0.03
Primary bile acid biosynthesis	46	0.58	1	4.50E-01	1.00E+00	1.00E+00	0.03
Purine metabolism	68	0.86	1	5.90E-01	1.00E+00	1.00E+00	0.00

Supplementary Table 2. AIF loss-mediated OXPHOS dysfunction induced metabolic adjustments in BM cells. Detailed results obtained in broad metabolic assessments of BM cells from 21-day-old AIF^{+Y} and AIF^{-Y} mice analyzed using the Metabolomics pathway (MetPA) software (freely available at <http://metpa.metabolomics.ca>). The data are expressed as the results recorded in the AIF^{-Y} cells compared to AIF^{+Y} cells. Statistical p values are as follows: (i) Total is the total number of compounds in a pathway; (ii) Hits represent the matched number from user uploaded data; (iii) Raw p is the original p-value calculated from the enrichment analysis; (iv) Holm p represents the p-value adjusted using the Holm-Bonferroni method; (v) FDR is the p-value adjusted using the False Discovery Rate; and (vi) Impact depicts the pathway impact value calculated based on a pathway topology analysis. In terms of impact, the metabolic pathways altered by the loss of AIF are shown in bold.