

Supplementary Table S1. Morphometric parameters and N₂ balance identified in weanling and young adult female Walker-256 tumour-bearing rats.

Morphometric parameters and N ₂ balance	Weanling				Young adult				F (DFn, DFd)			P-value		
	Control	Initial	Intermediated	Advanced	Control	Initial	Intermediated	Advanced	Interaction	Tumour evolution	Age	Interaction	Tumour evolution	Age
	Mean	Mean	Mean	Mean	Mean	Mean	Mean	Mean						
	± SD	± SD	± SD	± SD	± SD	± SD	± SD	± SD						
Initial weight (g)	51.25 ± 1.25	56.63 ± 5.67	60.47 ± 6.19	59.24 ± 3.98	256.16 ± 16.10	252.08 ± 11.91	241.45 ± 8.28	279.54 ± 9.95	11.89 (3, 45)	12.80 (3, 45)	6574.00 (1, 45)	<0.01	<0.01	<0.01
Final weight (g)	126.25 ± 2.63	85.35 ± 9.57	95.64 ± 10.36	115.11 ± 20.49	268.65 ± 14.88	254.50 ± 8.97	256.87 ± 6.95	282.37 ± 26.30	1.60 (3, 49)	11.31 (3, 49)	1239.00 (1, 49)	0.20	<0.01	<0.01
Δ Body weight (g)	75.00 ± 1.41	27.44 ± 5.27	32.19 ± 7.65	43.48 ± 14.22	12.48 ± 5.25	-9.90 ± 11.14	-12.90 ± 8.78	-19.38 ± 30.86	2.98 (3, 45)	17.22 (3, 45)	185.90 (1, 45)	0.04	<0.01	<0.01
Tumour weight (g)	--	1.27 ± 0.83	3.26 ± 1.92	8.52 ± 3.07	--	12.32 ± 2.39	28.32 ± 6.01	32.28 ± 13.81	5.65 (2.41)	20.19 (2, 41)	115.60 (1, 41)	0.01	<0.01	<0.01
Tumour relative weight (g)	--	0.02 ± 0.01	0.06 ± 0.03	0.14 ± 0.05	--	0.05 ± 0.01	0.12 ± 0.03	0.12 ± 0.05	3.78 (2, 39)	21.05 (2, 39)	2.96 (1, 39)	0.03	<0.01	0.09
Gastrocnemius weight (g)	0.74 ± 0.02	0.45 ± 0.04	0.47 ± 0.05	0.44 ± 0.12	1.93 ± 0.14	1.56 ± 0.45	1.22 ± 0.17	1.22 ± 0.36	3.50 (3, 49)	14.70 (3, 49)	268.30 (1, 49)	0.02	<0.01	<0.01
Gastrocnemius relative weight (g)	1.45 ± 0.02	0.81 ± 0.11	0.81 ± 0.15	0.70 ± 0.19	0.75 ± 0.05	0.62 ± 0.18	0.50 ± 0.05	0.45 ± 0.15	6.60 (3, 45)	27.25 (3, 45)	71.52 (1, 45)	<0.01	<0.01	<0.01
Food intake N ₂ (mg)	188.27 ± 33.52	146.97 ± 54.72	114.29 ± 62.83	37.98 ± 30.79	715.59 ± 202.79	401.73 ± 97.31	332.63 ± 85.55	139.00 ± 92.07	20.17 (3, 76)	56.06 (3, 76)	188.10 (1, 76)	<0.01	<0.01	<0.01
Urinary N ₂ (mg)	38.54 ± 28.61	47.13 ± 19.07	31.57 ± 17.50	16.22 ± 19.75	159.30 ± 69.63	181.23 ± 59.18	86.00 ± 30.78	127.44 ± 74.37	3.45 (3, 76)	7.11 (3, 76)	124.00 (1, 76)	0.02	<0.01	<0.01
Faecal N ₂ (mg)	19.19 ± 8.02	8.61 ± 5.72	6.00 ± 2.93	5.02 ± 3.55	33.54 ± 21.84	35.93 ± 14.14	25.35 ± 8.84	18.76 ± 12.65	1.78 (3, 76)	7.65 (3, 76)	63.36 (1, 76)	0.15	<0.01	<0.01

N ₂ balance (mg)	130.54 ± 35.48	101.17 ± 29.05	90.27 ± 37.94	16.75 ± 29.76	522.75 ± 169.80	184.57 ± 78.24	221.28 ± 76.11	-7.21 ± 45.68	30.48 (3, 74)	68.01 (3, 74)	81.43 (1, 74)	<0.01	<0.01	<0.01
N ₂ balance (%)	100.00 ± 27.18	77.50 ± 22.25	69.15 ± 29.07	12.83 ± 22.79	100.00 ± 32.48	35.31 ± 14.97	42.33 ± 14.56	-1.38 ± 8.74	3.03 (3, 74)	56.82 (3,74)	16.25 (1, 74)	0.03	<0.01	<0.01

Legend: Weanling and young adult female rats were distributed into control (WC and AC) and initial (WWi and AWi), intermediated (WWm and AWm) and advanced (WWa and AWa) Walker tumour-bearing. DF_n and DF_d: degrees of freedom for the numerator and denominator of the F ratio, respectively. Data were expressed as mean ± standard deviation (SD) and analysed by two-way ANOVA. Bold *P* values represented a significant difference.

Supplementary Table S2. Total gastrocnemius muscle metabolic profile identified in weanling and young adult female Walker-256 tumour-bearing rats.

Metabolite	Weanling				Young adult				F (DFn, DFd)			P-value		
	Control	Initial	Intermediated	Advanced	Control	Initial	Intermediated	Advanced	Interaction	Tumour evolution	Age	Interaction	Tumour evolution	Age
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD						
4-Pyridoxate	4.60 ± 1.40	3.73 ± 1.72	5.32 ± 2.82	7.60 ± 4.18	5.00 ± 2.52	9.27 ± 1.66	6.33 ± 2.94	18.92 ± 8.87	5.83 (3, 48)	13.53 (3, 48)	19.15 (1, 48)	<0.01	<0.01	<0.01
Acetate	7.75 ± 2.33	10.42 ± 4.31	12.17 ± 4.75	13.66 ± 4.25	6.67 ± 1.60	10.32 ± 3.39	5.35 ± 2.32	6.40 ± 1.10	3.38 (3, 49)	1.77 (3, 49)	13.57 (1, 49)	0.03	0.17	<0.01
ADP	9.20 ± 7.14	10.97 ± 3.86	22.25 ± 7.90	14.82 ± 7.20	8.87 ± 5.07	8.03 ± 1.13	7.51 ± 2.67	8.32 ± 4.24	3.37 (3, 48)	2.48 (3, 48)	13.08 (1, 48)	0.03	0.07	<0.01
Alanine	282.40 ± 90.89	278.28 ± 61.40	256.73 ± 90.73	281.50 ± 127.26	129.36 ± 24.02	148.33 ± 17.55	139.94 ± 31.63	193.21 ± 41.29	0.33 (3, 49)	0.58 (3, 49)	27.32 (1, 49)	0.80	0.63	<0.01
AMP	349.56 ± 105.97	302.10 ± 74.54	317.03 ± 127.16	315.61 ± 130.52	254.13 ± 76.33	328.20 ± 19.52	323.41 ± 96.75	430.20 ± 88.13	2.11 (3, 49)	1.22 (3, 49)	0.20 (1, 49)	0.11	0.31	0.66
Anserine	62.91 ± 44.75	84.07 ± 28.58	102.18 ± 14.38	89.37 ± 43.63	99.66 ± 62.67	188.39 ± 74.52	258.12 ± 191.55	256.59 ± 99.99	1.54 (3, 46)	3.62 (3, 46)	26.54 (1, 46)	0.21	0.02	<0.01
Carnosine	490.07 ± 160.53	264.40 ± 78.46	429.98 ± 92.40	317.31 ± 98.55	423.20 ± 113.28	474.55 ± 42.27	271.23 ± 158.08	700.95 ± 166.17	15.80 (3, 48)	5.68 (3, 48)	8.38 (1, 48)	<0.01	<0.01	<0.01
Choline	11.17 ± 2.77	13.35 ± 3.37	21.39 ± 4.64	27.45 ± 11.29	33.70 ± 11.79	26.12 ± 7.86	25.47 ± 16.73	26.52 ± 5.45	3.17 (3, 47)	1.14 (3, 47)	11.96 (1, 47)	0.03	0.34	<0.01
Creatine	2035.82 ± 660.75	1644.58 ± 487.87	2264.31 ± 570.31	2505.65 ± 684.57	1508.52 ± 367.35	1934.75 ± 242.49	1830.90 ± 565.41	2390.04 ± 480.99	1.38 (3, 49)	4.38 (3, 49)	1.60 (1, 49)	0.26	0.01	0.21
Cytidine	5.23 ± 1.57	2.97 ± 0.87	4.55 ± 1.17	6.86 ± 3.01	1.17 ± 0.22	1.87 ± 0.25	4.02 ± 2.13	5.61 ± 2.41	1.90 (3, 49)	10.31 (3, 49)	10.39 (1, 49)	0.14	<0.01	<0.01

Formate	3.33	3.24	3.93	5.93	2.36	3.19	2.68	2.51	1.57	0.99	5.61	0.21	0.41	0.02
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	1.09	3.34	2.08	2.23	0.81	2.05	1.48	0.87						
Fumarate	6.32	3.55	4.85	5.66	3.15	2.95	2.46	3.10	1.53	2.22	24.05	0.22	0.10	<0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	1.96	1.01	1.99	2.12	0.89	1.11	0.89	0.63						
Glucuronate	80.69	109.18	131.19	133.26	97.96	129.48	144.37	182.38	0.12	1.25	0.99	0.94	0.30	0.32
	±	±	±	±	±	±	±	±	(3, 48)	(3, 48)	(1, 48)			
	17.25	20.21	91.04	141.76	64.96	13.64	39.95	35.53						
Glutamate	160.08	168.54	91.91	84.62	41.81	62.41	52.51	78.96	6.97	3.67	42.87	<0.01	0.02	<0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	49.97	55.07	40.78	31.19	14.57	15.03	28.71	22.49						
Glutamine	347.71	272.07	182.32	131.51	98.90	126.15	82.26	97.63	4.16	5.96	39.08	0.01	<0.01	<0.01
	±	±	±	±	±	±	±	±	(3, 48)	(3, 48)	(1, 48)			
	71.82	86.09	107.58	75.39	37.26	19.58	17.53	44.92						
Glycine	306.49	372.54	318.74	217.11	90.47	118.03	80.60	139.28	1.33	0.63	28.20	0.27	0.60	<0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	116.97	175.83	179.18	152.58	19.07	10.07	19.53	27.95						
Histamine	2.17	1.63	1.58	2.54	0.65	1.09	0.70	0.79	1.83	1.14	30.81	0.15	0.34	<0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	0.67	0.80	0.81	1.04	0.41	0.48	0.21	0.20						
Histidine	1.88	1.28	1.02	1.83	0.37	0.33	0.28	0.18	0.71	0.61	20.65	0.55	0.61	<0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	0.59	0.60	0.48	1.74	0.36	0.20	0.14	0.05						
Imidazole	1.06	1.09	1.42	1.54	1.53	1.32	0.85	1.10	2.64	0.32	0.27	0.06	0.81	0.60
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	0.40	0.39	0.56	0.43	0.80	0.81	0.41	0.38						
Inosine	12.75	9.73	12.50	15.92	13.50	19.12	14.45	20.91	1.54	2.73	7.74	0.22	0.05	0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	4.18	2.88	4.48	7.77	4.95	6.27	3.67	4.13						
Isoleucine	6.11	6.52	8.58	11.24	5.12	7.38	7.86	11.81	0.34	10.74	0.01	0.80	<0.01	0.93
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	1.96	2.13	3.24	3.19	1.24	1.27	3.39	3.88						
Lactate	1997.95	1950.12	2664.32	2692.80	2356.89	3368.42	2619.18	3705.32	1.92	3.02	8.20	0.14	0.04	0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	687.93	737.34	1108.03	981.74	701.73	415.28	820.11	582.62						

Leucine	10.66	11.85	15.05	23.90	7.44	10.51	11.69	16.23						
	±	±	±	±	±	±	±	±	1.16	13.82	8.78	0.34	<0.01	<0.01
	3.96	3.68	3.80	7.08	1.77	1.99	3.76	4.60	(3, 49)	(3, 49)	(1, 49)			
Lysine	144.78	131.18	151.64	139.42	52.15	59.46	61.30	90.69						
	±	±	±	±	±	±	±	±	0.38	0.29	19.81	0.77	0.83	<0.01
	55.63	67.08	82.74	75.30	17.70	4.81	24.56	30.74	(3, 49)	(3, 49)	(1, 49)			
Maltose	8.30	8.55	7.47	12.47	5.13	8.37	7.78	6.02						
	±	±	±	±	±	±	±	±	0.35	0.16	0.84	0.78	0.92	0.36
	5.18	3.37	5.16	15.69	1.86	5.19	3.10	0.60	(3, 47)	(3, 47)	(1, 47)			
Methionine	7.07	8.28	7.40	9.26	4.50	7.48	6.82	8.27						
	±	±	±	±	±	±	±	±	0.29	2.44	2.44	0.83	0.08	0.12
	2.15	3.43	2.82	1.91	2.11	3.59	3.25	3.39	(3, 49)	(3, 49)	(1, 49)			
myo-Inositol	37.35	45.32	50.78	43.84	15.68	15.57	21.95	20.84						
	±	±	±	±	±	±	±	±	0.34	1.41	55.06	0.79	0.24	<0.01
	14.26	7.86	14.68	15.64	4.03	3.57	9.67	6.90	(3, 47)	(3, 47)	(1, 47)			
N,N-Dimethylglycine	5.06	4.07	5.83	6.06	1.60	1.47	1.05	0.61						
	±	±	±	±	±	±	±	±	2.82	0.61	106.60	0.05	0.61	<0.01
	1.62	1.12	1.75	1.46	1.57	1.25	1.13	0.31	(3, 49)	(3, 49)	(1, 49)			
NAD+	13.98	9.89	9.85	5.52	6.56	3.17	3.19	2.99						
	±	±	±	±	±	±	±	±	0.88	3.50	21.67	0.45	0.02	<0.01
	4.61	3.63	4.14	4.15	7.69	1.16	2.36	0.72	(3, 48)	(3, 48)	(1, 48)			
NADP+	14.83	11.38	10.02	4.48	0.99	1.03	1.44	0.62						
	±	±	±	±	±	±	±	±	4.32	5.06	96.23	<0.01	<0.01	<0.01
	4.71	4.09	4.07	2.91	0.48	0.71	1.50	0.10	(3, 46)	(3, 46)	(1, 46)			
Niacinamide	13.18	13.51	16.64	24.87	14.60	20.33	20.69	26.77						
	±	±	±	±	±	±	±	±	0.42	7.39	3.49	0.74	<0.01	0.07
	4.09	6.35	7.28	7.78	4.47	5.58	8.67	5.50	(3, 49)	(3, 49)	(1, 49)			
Nicotinurate	3.35	5.16	6.73	8.24	8.31	8.49	10.36	11.35						
	±	±	±	±	±	±	±	±	0.14	2.87	13.03	0.93	0.05	<0.01
	1.57	2.92	3.18	5.65	2.64	2.65	2.43	2.52	(3, 49)	(3, 49)	(1, 49)			
N-Methylhydantoin	3.25	2.96	3.99	4.78	10.04	11.14	11.56	14.43						
	±	±	±	±	±	±	±	±	1.12	5.44	192.90	0.35	<0.01	<0.01
	1.08	1.81	1.19	1.42	2.95	0.93	3.69	2.67	(3, 49)	(3, 49)	(1, 49)			
O-Acetylcarnitine	9.23	15.80	10.39	17.76	12.38	11.34	12.13	12.02						
	±	±	±	±	±	±	±	±	3.01	2.35	1.08	0.04	0.08	0.30
	3.02	5.21	3.51	5.24	3.31	3.89	6.41	2.32	(3, 49)	(3, 49)	(1, 49)			

Phenylalanine	4.80	4.99	8.83	12.63	5.53	9.09	9.38	13.94	0.99	17.83	3.99	0.41	<0.01	0.05
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	1.44	1.61	2.50	3.98	1.51	1.25	3.63	4.63						
Pyridoxine	2.66	0.89	2.16	1.51	2.33	3.40	4.16	6.06	3.85	2.26	18.90	0.01	0.09	<0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	0.80	0.65	1.48	0.69	1.77	0.59	3.22	3.96						
sn-Glycero-3-phosphocholine	8.85	8.82	7.95	10.36	9.29	14.17	17.61	15.81	3.01	2.56	24.16	0.04	0.07	<0.01
	±	±	±	±	±	±	±	±	(3, 46)	(3, 46)	(1, 46)			
	2.48	4.56	2.72	2.36	2.25	3.23	5.66	4.89						
Succinate	60.01	40.94	32.80	29.57	11.56	2.96	3.35	4.30	1.03	2.78	51.52	0.39	0.05	<0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	24.16	24.22	14.69	21.75	11.53	0.99	1.79	1.34						
Taurine	1005.47	667.40	978.88	894.52	760.44	1036.75	901.59	1068.94	3.87	0.79	0.68	0.01	0.50	0.41
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	174.86	176.18	252.78	291.76	225.21	202.74	162.11	271.30						
Theophylline	1.51	2.62	1.56	1.95	0.88	1.80	0.87	2.41	0.66	2.23	1.19	0.58	0.10	0.28
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	1.02	2.43	1.01	1.23	0.30	1.16	0.35	1.27						
Tryptophan	2.03	2.16	3.05	3.38	1.27	1.58	1.40	2.30	0.97	4.84	17.99	0.42	0.01	<0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	0.63	0.59	1.04	1.19	0.30	0.39	0.26	1.02						
Tyrosine	9.39	8.60	11.99	15.98	5.95	9.81	10.24	14.46	0.55	6.98	1.19	0.65	<0.01	0.28
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	2.82	2.38	3.45	6.66	1.31	1.24	5.88	5.28						
UDP-glucuronate	12.25	7.46	10.74	13.12	4.33	7.49	8.25	13.02	1.64	3.52	3.62	0.19	0.02	0.06
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	5.34	3.63	3.59	6.83	1.15	1.62	5.90	5.95						
UDP-N-Acetylglucosamine	5.13	4.00	5.85	3.80	1.45	1.66	3.80	2.79	0.44	1.21	7.91	0.72	0.32	0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(3, 49)			
	4.03	1.93	3.52	2.47	0.36	0.71	4.83	3.47						
Uracil	2.58	2.26	2.67	4.64	0.57	1.14	1.07	1.38	1.63	3.26	27.88	0.19	0.03	<0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	1.18	0.54	0.88	2.46	0.25	0.29	0.47	0.22						
Valine	12.15	13.83	15.49	19.80	8.82	12.26	11.68	16.06	0.25	8.57	8.51	0.86	<0.01	0.01
	±	±	±	±	±	±	±	±	(3, 49)	(3, 49)	(1, 49)			
	3.80	2.97	3.08	5.08	1.91	3.03	4.45	3.68						

Xanthine	6.22 ± 2.01	3.26 ± 1.89	1.79 ± 1.01	4.56 ± 2.44	1.12 ± 0.30	2.27 ± 1.27	0.91 ± 0.20	0.79 ± 0.32	4.97 (3, 49)	4.12 (3, 49)	34.42 (1, 49)	<0.01	0.01	<0.01
π-Methylhistidine	8.64 ± 5.82	24.43 ± 13.20	20.53 ± 6.79	21.61 ± 13.86	6.29 ± 4.16	19.10 ± 6.18	2.23 ± 1.98	1.25 ± 0.21	2.58 (3, 48)	4.73 (3, 48)	16.99 (1, 48)	0.06	<0.01	<0.01
τ-Methylhistidine	2.65 ± 3.14	1.93 ± 1.02	2.27 ± 0.66	1.61 ± 0.71	1.23 ± 0.59	1.10 ± 0.83	1.33 ± 0.82	1.15 ± 0.80	0.39 (3, 49)	0.67 (3, 49)	8.80 (1, 49)	0.76	0.57	<0.01

Legend: Weanling and young adult female rats were distributed into control (WC and AC) and initial (WWi and AWi), intermediated (WWm and AWm) and advanced (WWa and AWa) Walker tumour-bearing. DFn and DFd: degrees of freedom for the numerator and denominator of the F ratio, respectively. Data were expressed as mean ± standard deviation (SD) (mM/ mg tissue) and analysed by two-way ANOVA. Bold *P* values represented a significant difference.