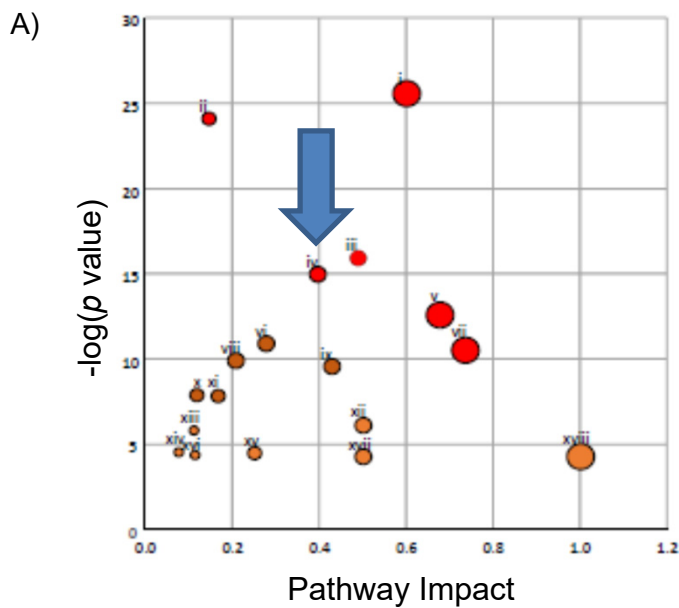
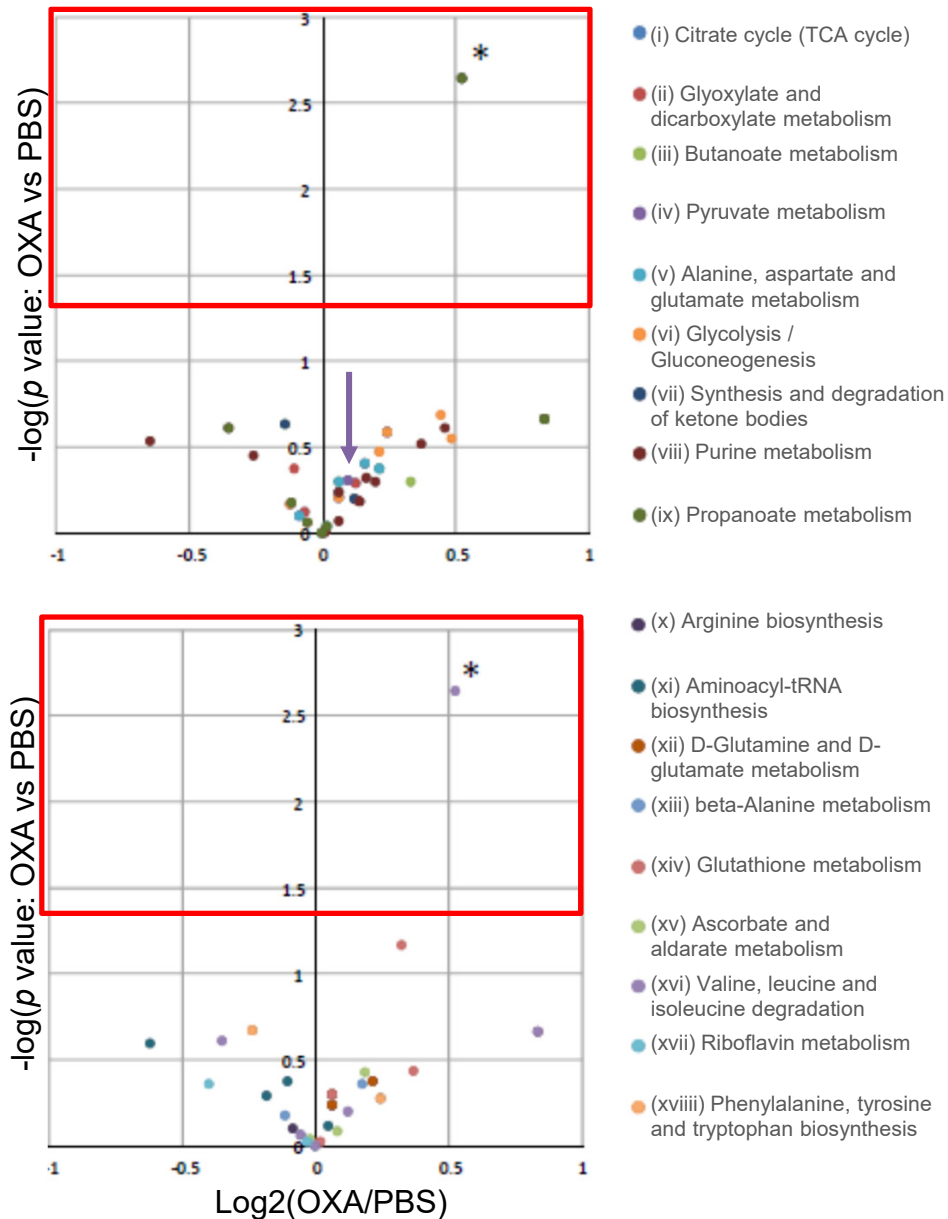


Suppl Fig. S1

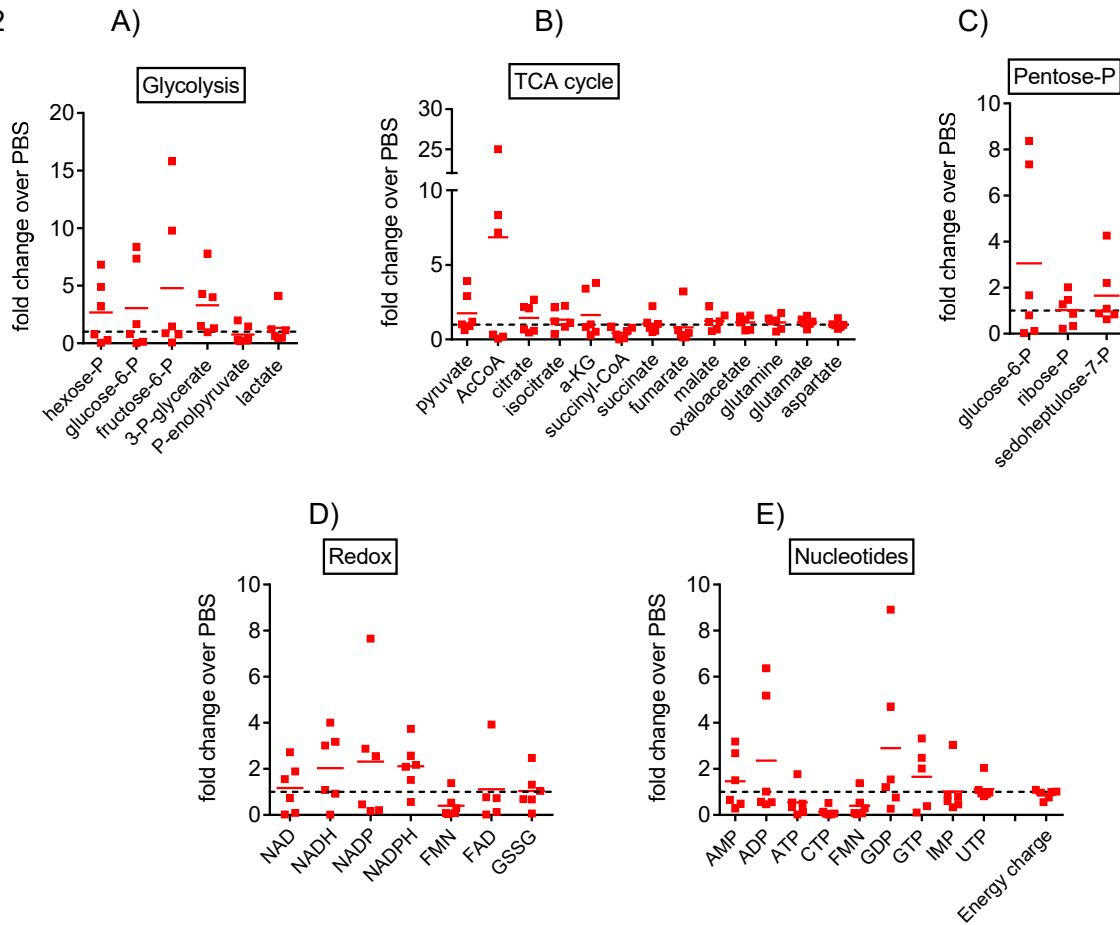


B)



1 **Supplementary Figure S1: Pathway analysis of metabolites extracted from pulverized long bone of oxamate-**
2 **and PBS-treated mice.** A) Metaboanalyst pathway analysis of metabolites was used to determine which metabolic
3 pathways have significant detection to warrant further discussion. The top 18 most covered pathways are shown and
4 listed as roman numerals from i-xviii (1-18) with i having the greatest metabolite coverage and xviii having the least.
5 (Arrow indicated pyruvate metabolism (iv); B) Volcano plot of metabolites from OXA- and PBS-treated mice from top
6 nine (i-ix, above) and bottom nine (x- xviii, below). Data on log base 10 scale has significance for p -value < 0.05 at >1.3
7 on the y-axis, and significant fold change > 3 at > 0.43 and < -0.43 on the x-axis. *, $p < 0.05$ vs PBS-treated controls (t -
8 test). Arrow marks location of pyruvate.
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Suupl Fig. S2



Supplementary Figure S2: Metabolite content following treatment with oxamate. Levels of metabolites extracted from long bone of mice treated with OXA or PBS are compared for central metabolic pathways revealing large but non-significant increases in glycolysis (A), TCA cycle (B), Pentose-phosphate pathway (C). Key Redox metabolites (D), and Nucleotides (E) were also increased after OXA treatment but did not reach significance. Data are expressed as fold change over the control (PBS-treated) levels marked with dotted lines. Plots show actual data points and calculated means. Significance was determined by unpaired *t*-test.

Table S1: Levels of metabolites assigned to specific pathways using Metaboanalyst in oxamate- vs PBS-treated mouse long bones

	Mean PBS	Mean OXA	SD PBS	SD OXA	p Value PBS vs OXA	FoldChange PBS vs OXA	-Log(p Value) PBS vs OXA	Log(FC) PBS vs OXA
(i) Citrate cycle (TCA cycle):								
alpha-Ketoglutarate_(a-KG)	26217.7586	43007.129	18629.23	40418.29	0.41689392	1.640381599	0.379974434	0.214944889
Succinyl-CoA	116.168071	51.40781	118.6868	41.92338	0.24033978	0.442529597	0.619174346	-0.354057678
Succinate	331334.172	345653.73	145225.6	209980.9	0.90058147	1.043217873	0.045476994	0.018375019
Isocitrate	10519.6499	13984.723	8955.897	7769.424	0.50880749	1.32939057	0.293446503	0.123652594
Oxaloacetate	18426.6949	21269.656	9829.662	8118.1	0.61134956	1.154284922	0.213710393	0.062313022
Malate	553127.034	688896.35	270659.4	339397.1	0.48887541	1.245457742	0.310801809	0.095328997
Aconitate	188415.706	162498.24	81495.33	154443	0.7443929	0.86244532	0.128197776	-0.06426843
Citrate	7949.98436	11510.718	4636.545	7726.802	0.39174292	1.447891893	0.406998844	0.160736136
Pyruvate	31420.2022	55284.016	12036.37	41950.97	0.25317457	1.759505405	0.596579913	0.245390605
Fumarate	40372.5888	33057.552	31940.29	48327.33	0.77935033	0.818811792	0.108267275	-0.086815911
Acetyl-CoA	172.896092	1185.2564	125.2373	1667.867	0.2125213	6.855310625	0.672597539	0.836027138
Phosphoenolpyruvate	1740.17645	1318.5497	1776.559	1337.978	0.66355503	0.757710361	0.178123057	-0.120496774
(ii) Glyoxylate and dicarboxylate metabolism:								
Aconitate	188415.706	162498.24	81495.33	154443	0.7443929	0.86244532	0.128197776	-0.06426843
Citrate	7949.98436	11510.718	4636.545	7726.802	0.39174292	1.447891893	0.406998844	0.160736136
Malonyl-CoA	513.939349	391.77518	419.2507	460.1548	0.65920326	0.762298481	0.180980657	-0.117874946
Methylmalonyl-CoA	3524.80607	3508.0416	3041.222	2588.283	0.9923229	0.995243871	0.003346984	-0.002070488
Propanoyl-CoA	85.9984913	75.723249	78.23899	106.1157	0.86182358	0.880518336	0.064581626	-0.055261596
Serine	40596.6326	31764.305	22566.05	10833.07	0.41510451	0.782436934	0.381842546	-0.106550657
Glutamate	359805.802	416065.25	151673.5	111283.3	0.49544774	1.156360586	0.30500215	0.063093281
Isocitrate	10519.6499	13984.723	8955.897	7769.424	0.50880749	1.32939057	0.293446503	0.123652594
Pyruvate	31420.2022	55284.016	12036.37	41950.97	0.25317457	1.759505405	0.596579913	0.245390605
Oxaloacetate	18426.6949	21269.656	9829.662	8118.1	0.61134956	1.154284922	0.213710393	0.062313022
Acetoacetyl-CoA	57.9540688	194.53479	51.26006	55.30617	0.00226476	3.356706408	2.644978152	0.525913358
Succinyl-CoA	116.168071	51.40781	118.6868	41.92338	0.24033978	0.442529597	0.619174346	-0.354057678
Glutamine	167078.921	193131.89	72189.35	75571.31	0.57567025	1.155932107	0.239826216	0.062932327
(iii) Butanoate metabolism:								
3-Hydroxybutyrate	52478.5453	38100.943	17519.82	19244.33	0.2313414	0.726028956	0.63574664	-0.139046058
Acetoacetate	35661.8554	46962.449	24244.05	43529.17	0.61905889	1.316881829	0.208268036	0.119546805
Acetyl-CoA	172.896092	1185.2564	125.2373	1667.867	0.2125213	6.855310625	0.672597539	0.836027138
Acetoacetyl-CoA	57.9540688	194.53479	51.26006	55.30617	0.00226476	3.356706408	2.644978152	0.525913358
Glutamate	359805.802	416065.25	151673.5	111283.3	0.49544774	1.156360586	0.30500215	0.063093281
Butyryl-CoA	132.538298	285.82225	70.18592	474.2739	0.49574709	2.156525717	0.304739825	0.333754642
alpha-Ketoglutarate_(a-KG)	26217.7586	43007.129	18629.23	40418.29	0.41689392	1.640381599	0.379974434	0.214944889
Succinate	331334.172	345653.73	145225.6	209980.9	0.90058147	1.043217873	0.045476994	0.018375019
(iv) Pyruvate metabolism:								
Oxaloacetate	18426.6949	21269.656	9829.662	8118.1	0.61134956	1.154284922	0.213710393	0.062313022
Phosphoenolpyruvate	1740.17645	1318.5497	1776.559	1337.978	0.66355503	0.757710361	0.178123057	-0.120496774
Pyruvate	31420.2022	55284.016	12036.37	41950.97	0.25317457	1.759505405	0.596579913	0.245390605
Malate	553127.034	688896.35	270659.4	339397.1	0.48887541	1.245457742	0.310801809	0.095328997
Lactate	3867286.31	5192042.7	2664038	5409687	0.63141026	1.342554519	0.199688363	0.127931931
Acetyl-CoA	172.896092	1185.2564	125.2373	1667.867	0.2125213	6.855310625	0.672597539	0.836027138
Acetoacetyl-CoA	57.9540688	194.53479	51.26006	55.30617	0.00226476	3.356706408	2.644978152	0.525913358
Malonyl-CoA	513.939349	391.77518	419.2507	460.1548	0.65920326	0.762298481	0.180980657	-0.117874946
Fumarate	40372.5888	33057.552	31940.29	48327.33	0.77935033	0.818811792	0.108267275	-0.086815911
(v) Alanine, aspartate and glutamate metabolism:								
Aspartate	256854.861	254868.66	171377.9	63477.25	0.97941746	0.992267227	0.009032156	-0.003371352
Glutamate	359805.802	416065.25	151673.5	111283.3	0.49544774	1.156360586	0.30500215	0.063093281
Glutamine	167078.921	193131.89	72189.35	75571.31	0.57567025	1.155932107	0.239826216	0.062932327
Citrate	7949.98436	11510.718	4636.545	7726.802	0.39174292	1.447891893	0.406998844	0.160736136
Oxaloacetate	18426.6949	21269.656	9829.662	8118.1	0.61134956	1.154284922	0.213710393	0.062313022
Fumarate	40372.5888	33057.552	31940.29	48327.33	0.77935033	0.818811792	0.108267275	-0.086815911
Pyruvate	31420.2022	55284.016	12036.37	41950.97	0.25317457	1.759505405	0.596579913	0.245390605
Succinate	331334.172	345653.73	145225.6	209980.9	0.90058147	1.043217873	0.045476994	0.018375019
alpha-Ketoglutarate_(a-KG)	26217.7586	43007.129	18629.23	40418.29	0.41689392	1.640381599	0.379974434	0.214944889
(vi) Glycolysis / Gluconeogenesis:								
Pyruvate	31420.2022	55284.016	12036.37	41950.97	0.25317457	1.759505405	0.596579913	0.245390605
Acetyl-CoA	172.896092	1185.2564	125.2373	1667.867	0.2125213	6.855310625	0.672597539	0.836027138
Lactate	3867286.31	5192042.7	2664038	5409687	0.63141026	1.342554519	0.199688363	0.127931931

1									
2	Phosphoenolpyruvate	1740.17645	1318.5497	1776.559	1337.978	0.66355503	0.757710361	0.178123057	-0.120496774
3	Glucose-6-Phosphate	14417.1558	44081.962	19230.71	54512.99	0.27985101	3.057604611	0.553073124	0.485381325
4	Glucose-1-Phosphate	11033.9012	30700.405	8860.87	30776.02	0.20355587	2.782370811	0.691316359	0.444415009
5	Oxaloacetate	18426.6949	21269.656	9829.662	8118.1	0.61134956	1.154284922	0.213710393	0.062313022
6	Dihydroxyacetone-Phosphate_/	15451.5741	25399.01	14376.32	17343.5	0.33398996	1.643781419	0.476266594	0.215844067
7	<u>(vii) Synthesis and degradation of ketone bodies:</u>								
8	Acetoacetyl-CoA	57.9540688	194.53479	51.26006	55.30617	0.00226476	3.356706408	2.644978152	0.525913358
9	Acetyl-CoA	172.896092	1185.2564	125.2373	1667.867	0.2125213	6.855310625	0.672597539	0.836027138
10	3-Hydroxybutyrate	52478.5453	38100.943	17519.82	19244.33	0.2313414	0.726028956	0.63574664	-0.139046058
11	Acetoacetate	35661.8554	46962.449	24244.05	43529.17	0.61905889	1.316881829	0.208268036	0.119546805
12	<u>(viii) Purine metabolism:</u>								
13	Guanosine_Diphosphate_(GDP)	812.978555	2353.2032	232.6867	2711.925	0.24119865	2.894545266	0.617625134	0.461580346
14	Xanthine	310914.762	490957.82	230603	529211.6	0.50023423	1.579075295	0.300826595	0.198402839
15	Ribose-5-Phosphate_/Ribulose	36395.0716	37586.29	32729.75	25183.51	0.94700322	1.03273021	0.023648542	0.013986881
16	Glutamine	167078.921	193131.89	72189.35	75571.31	0.57567025	1.155932107	0.239826216	0.062932327
17	Adenosine_Diphosphate_(ADP)	60498.3794	142534.55	34710.13	162248.1	0.29975176	2.356006056	0.523238257	0.372176402
18	Adenosine_Monophosphate_(AI	42628.2603	62445.334	30563.7	52108.66	0.47460324	1.464881119	0.323669301	0.165802381
19	Adenosine_Triphosphate_(ATP)	8676.64023	4760.3464	7649.34	5500.175	0.34875844	0.548639367	0.45747528	-0.260713033
20	Xanthosine	13406.5765	3023.0438	22048.05	4861.308	0.28660785	0.225489619	0.542711917	-0.646873447
21	Hypoxanthine	261533.893	302674.48	255649.9	383270	0.84270773	1.157304977	0.074323024	0.063447821
22	Inosine	1999919.46	2029097.9	1711555	2028036	0.98025694	1.014589827	0.008660073	0.006290504
23	Guanosine_Triphosphate_(GTP)	126.198959	174.28923	147.4333	177.5802	0.64150051	1.381067102	0.192802994	0.14021478
24	<u>(ix) Propanoate metabolism:</u>								
25	Methylmalonyl-CoA	3524.80607	3508.0416	3041.222	2588.283	0.9923229	0.995243871	0.003346984	-0.002070488
26	Succinate	331334.172	345653.73	145225.6	209980.9	0.90058147	1.043217873	0.045476994	0.018375019
27	Propanoyl-CoA	85.9984913	75.723249	78.23899	106.1157	0.86182358	0.880518336	0.064581626	-0.055261596
28	Acetyl-CoA	172.896092	1185.2564	125.2373	1667.867	0.2125213	6.855310625	0.672597539	0.836027138
29	Malonyl-CoA	513.939349	391.77518	419.2507	460.1548	0.65920326	0.762298481	0.180980657	-0.117874946
30	Succinyl-CoA	116.168071	51.40781	118.6868	41.92338	0.24033978	0.442529597	0.619174346	-0.354057678
31	Acetoacetyl-CoA	57.9540688	194.53479	51.26006	55.30617	0.00226476	3.356706408	2.644978152	0.525913358
32	<u>(x) Arginine biosynthesis:</u>								
33	Glutamate	359805.802	416065.25	151673.5	111283.3	0.49544774	1.156360586	0.30500215	0.063093281
34	Aspartate	256854.861	254868.66	171377.9	63477.25	0.97941746	0.992267227	0.009032156	-0.003371352
35	Glutamine	167078.921	193131.89	72189.35	75571.31	0.57567025	1.155932107	0.239826216	0.062932327
36	alpha-Ketoglutarate_(a-KG)	26217.7586	43007.129	18629.23	40418.29	0.41689392	1.640381599	0.379974434	0.214944889
37	Fumarate	40372.5888	33057.552	31940.29	48327.33	0.77935033	0.818811792	0.108267275	-0.086815911
38	<u>(xi) Aminoacyl-tRNA biosynthesis:</u>								
39	Phenylalanine	8962.16318	5173.4382	6599.869	1908.18	0.20902904	0.577253291	0.679793367	-0.238633583
40	Glutamine	167078.921	193131.89	72189.35	75571.31	0.57567025	1.155932107	0.239826216	0.062932327
41	Aspartate	256854.861	254868.66	171377.9	63477.25	0.97941746	0.992267227	0.009032156	-0.003371352
42	Serine	40596.6326	31764.305	22566.05	10833.07	0.41510451	0.782436934	0.381842546	-0.106550657
43	Methionine	5458.49439	3556.2931	4447.236	4680.917	0.50993013	0.651515387	0.292489322	-0.186075323
44	Threonine	81129.6698	90634.611	49818.2	48821.23	0.75729209	1.117157395	0.120736582	0.048114365
45	Tryptophan	227.294652	53.8864	348.2006	28.63966	0.25042208	0.237077289	0.601327386	-0.625110048
46	Tyrosine	2963.90306	5174.027	3373.105	6668.386	0.52025535	1.745680247	0.283783448	0.241964698
47	Glutamate	359805.802	416065.25	151673.5	111283.3	0.49544774	1.156360586	0.30500215	0.063093281
48	<u>(xii) D-Glutamine and D-glutamate metabolism:</u>								
49	Glutamate	359805.802	416065.25	151673.5	111283.3	0.49544774	1.156360586	0.30500215	0.063093281
50	Glutamine	167078.921	193131.89	72189.35	75571.31	0.57567025	1.155932107	0.239826216	0.062932327
51	alpha-Ketoglutarate_(a-KG)	26217.7586	43007.129	18629.23	40418.29	0.41689392	1.640381599	0.379974434	0.214944889
52	<u>(xiii) beta-Alanine metabolism:</u>								
53	Propanoyl-CoA	85.9984913	75.723249	78.23899	106.1157	0.86182358	0.880518336	0.064581626	-0.055261596
54	Malonyl-CoA	513.939349	391.77518	419.2507	460.1548	0.65920326	0.762298481	0.180980657	-0.117874946
55	Aspartate	256854.861	254868.66	171377.9	63477.25	0.97941746	0.992267227	0.009032156	-0.003371352
56	Carnosine	128592.704	192689.24	90681.6	153165.7	0.43371826	1.498446103	0.362792295	0.175641127
57	Acetyl-CoA	172.896092	1185.2564	125.2373	1667.867	0.2125213	6.855310625	0.672597539	0.836027138
58	<u>(xiv) Glutathione metabolism:</u>								
59	NADP+_Oxidized	2735.23685	6331.141	2876.165	7867.272	0.36091768	2.314659154	0.442591846	0.364487048
60	Glutathione_oxidized_(GSSG)	604964.474	628066.86	510864.9	494538	0.9410648	1.038187996	0.026380469	0.016276003
	NADPH_Reduced	836.327352	1762.1595	488.1627	887.6471	0.06795902	2.107021262	1.167752902	0.323668918

