

Targeted metabolic profiling of the Tg197 mouse model reveals itaconic acid as a marker of Rheumatoid Arthritis.

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Table S1: Table S1: List of animals per group

Table S2: Metabolite list profiled at all biospecimens with the targeted LC-MS platform

Figure S1: (A) Mouse body weight trajectory and (B) arthritic score across 6 weeks of *in vivo* study.

Figure S2: Itaconic acid median peak area distribution at serum and urine samples collected at week 6 and 11 of age.

Figure S3: Detailed representation of citrate to α-ketoglutarate metabolism with associated enzyme located in the cytoplasm and mitochondrion.

Supplementary Tables

Table S2: List of animals per group.

Group	Urine (Study 1)	Serum (Study 1)	SF (study 2)	Urine (Study 3)	Serum (Study3)
	Week6	Week6	Week 6	Week 6	Week 6
Male Tg197	7	7	7	6	6
Female Tg197			7	6	5
Male WT	7	7	7	6	6
Female WT			8	6	6
	Weeks 7-11*	Week11	Week11	Week 11	Week 11
Male Tg197	7	7	5	3	5
Female Tg197				4	3
Male WT	7	7	5	5	5
Female WT				3	5
Male Tr	7	7	5	6	6
Female Tr				4	5

* urine collection performed on weekly basis

Table S2: Metabolites profiled in all biospecimens with the targeted LC-MS platform

Number	ID	Metabolite Name
1	AcetylCoA	Acetyl coenzymeA
2	Adenine	Adenine
3	Adipic acid	Adipic acid
4	ADP	Adenosine diphosphate
5	ADP ribose	Adenosine diphosphate ribose
6	α KET	α -ketoglutaric acid
7	AMP dGMP	Adenosine monophosphate or 2'-deoxyguanosine monophosphate
8	Arginine	Arginine
9	Asparagine	Asparagine
10	Aspartic acid	Aspartic acid
11	ATP	Adenosine triphosphate
12	Benzoic acid	Benzoic acid
13	cAMP	Adenosine-3'5'- cyclic monophosphate
14	cGMP	Guanosine-3'5'-cyclic monophosphate
15	cis aconitic acid	<i>cis</i> Aconitic acid
16	Citrate	Citric acid
17	Citrulline	Citrulline
18	CMP	Cytidine monophosphate
19	Coumaric acid	Coumaric acid
20	Creatine	Creatine
21	Creatinine	Creatinine
22	Cystine	Cystine
23	Cytosine	Cytosine
24	dADP	2'-deoxyadenosine diphosphate
25	dAMP	2'-deoxyadenosine monophosphate
26	dATP	2'-deoxyadenosine triphosphate
27	dCDP	2'-deoxycytidine diphosphate
28	dCMP	2'-deoxycytidine monophosphate

Number	ID	Metabolite Name
29	dCTP	2'-deoxycytidine triphosphate
30	dinitrosalicylic acid	Dinitrosalicylic acid
31	FAD	Flavin-adenine-dinucleotide
32	FBP	Fructose 1,6 bisphosphate
33	Ferrulic acid	Ferrulic acid
34	Folate	Folic acid
35	Fructose 1 P	Fructose 1 P
36	Fructose 6 P	Fructose 6 P
37	Fumaric acid	Fumaric acid
38	G3P	Glycerate 3 phosphate
39	GAP	Glyceraldehyde-3-phosphate
40	GBP	Glycerate 1,3 bisphosphate
41	GDP	Guanosine diphosphate
42	Glucosamine6P	Glucosamine 6 phosphate
43	Glucose 1 P	Glucose 1 P
44	Glucose 6 P	Glucose 6 P
45	Glucuronic acid	Glucuronic acid
46	Glutamate	Glutamic acid
47	Glutamine	Glutamine
48	Glutaric acid	Glutaric acid
49	Glutathione ox	Glutathione oxidised
50	Glutathione red	Glutathione reduced
51	Glyoxylic acid	Glyoxylic acid
52	GMP	Guanosine monophosphate
53	GTP	Guanosine triphosphate
54	Guanine	Guanine
55	Guanosine	Guanosine
56	Histidine	Histidine
57	HPPA	Hydroxyphenyl propionic acid
58	ICA	Indole-2-carboxylic acid

Number	ID	Metabolite Name
59	IMP	Inosine monophosphate
60	inosine	Inosine
61	Isocitrate	Isocitric acid
62	Isoleucine	Isoleucine
63	Itaconic acid	Itaconic acid
64	Lactate	Lactic acid
65	Leucine	Leucine
66	Maleic acid	Maleic acid
67	Malic acid	Malic acid
68	Malonic acid	Malonic acid
69	Malonyl CoA	Malonyl coenzymeA
70	Mannose 6 P	Mannose 6 P
71	Methionine	Methionine
72	Methyl_Malonyl_CoA	Methyl malonyl coenzymeA
73	Methylxanthine	Methylxanthine
74	NAD	Nicotinamide Adenine Dinucleotide
75	NADH	Nicotinamide Adenine Dinucleotide reduced
76	NADP	Nicotinamide Adenine Dinucleotide Phosphate
77	NADPH	Nicotinamide Adenine Dinucleotide Phosphate reduced
78	NAG	N-acetylglucosamine
79	Nicotinic acid	Nicotinic acid
80	Nitrophenol	Nitrophenol
81	Orotic acid	Orotic acid
82	Pantothenic acid	Pantothenic acid
83	Pcreatine	Phosphocreatine
84	PEP	Phosphoenol pyruvic acid
85	PG	6-phosphogluconic acid
86	phenylalanine	Phenylalanine
87	Phthalic acid	Phthalic acid
88	Proline	Proline

Number	ID	Metabolite Name
89	Pserine	Phosphoserine
90	Pyruvate	Pyruvic acid
91	R5P	Ribose 5 phosphate
92	riboflavin	Riboflavin
93	Salicylic acid	Salicylic acid
94	Serine	Serine
95	Shikimic acid	Shikimic acid
96	sorbitol mannitol	sorbitol mannitol
97	Succinate	Succinic acid
98	Threonine	Threonine
99	Thymine	Thymine
100	TIA	2-trans-3-indolepyruvic acid
101	Tryptophan	Tryptophan
102	Tyrosine	Tyrosine
103	UDP	Uridine diphosphate
104	UDP glucA	Uridine diphosphate glucuronic acid
105	UDP glucose	Uridine diphosphate glucose
106	UMP	Uridine monophosphate
107	Uracil	Uracil
108	Uridine	Uridine
109	Valine	Valine

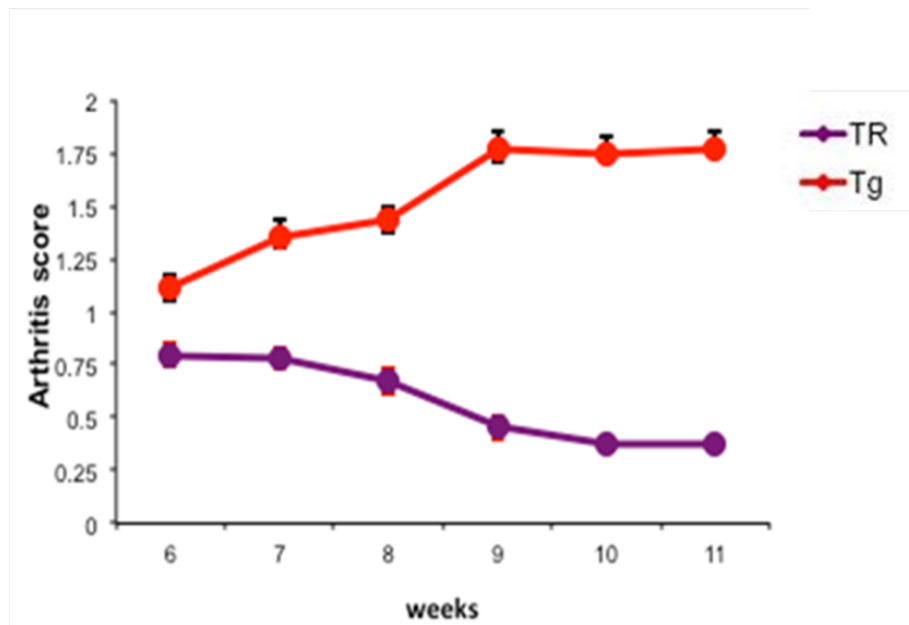
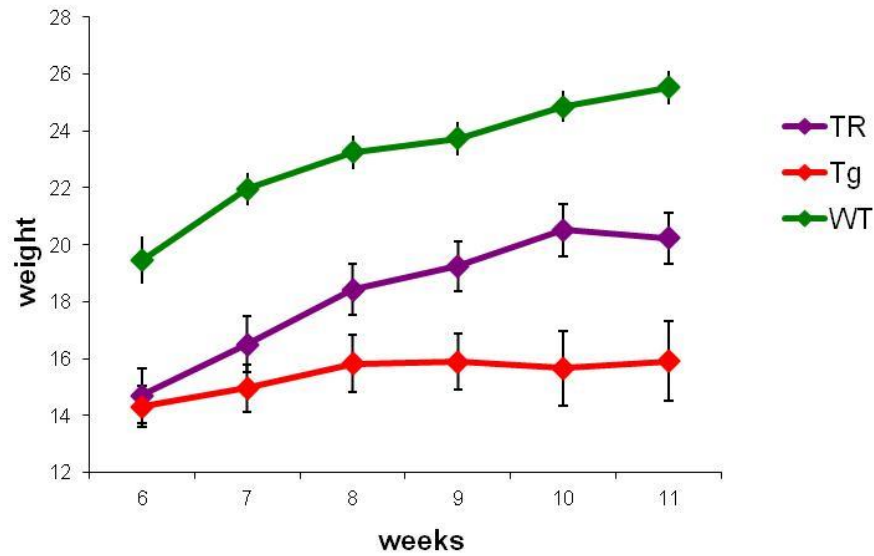


Figure S1: (A) Mouse body weight trajectory and (B) arthritic score across 6 weeks of *in vivo* study. Healthy control (WT), diseased (TG) and treated with 10mg/Kg Infliximab animals (TR). Vertical lines represent the body weight variability across a number of animals per groups across the course of the *in vivo* study starting at week 6 up to week 11 of the mouse age.

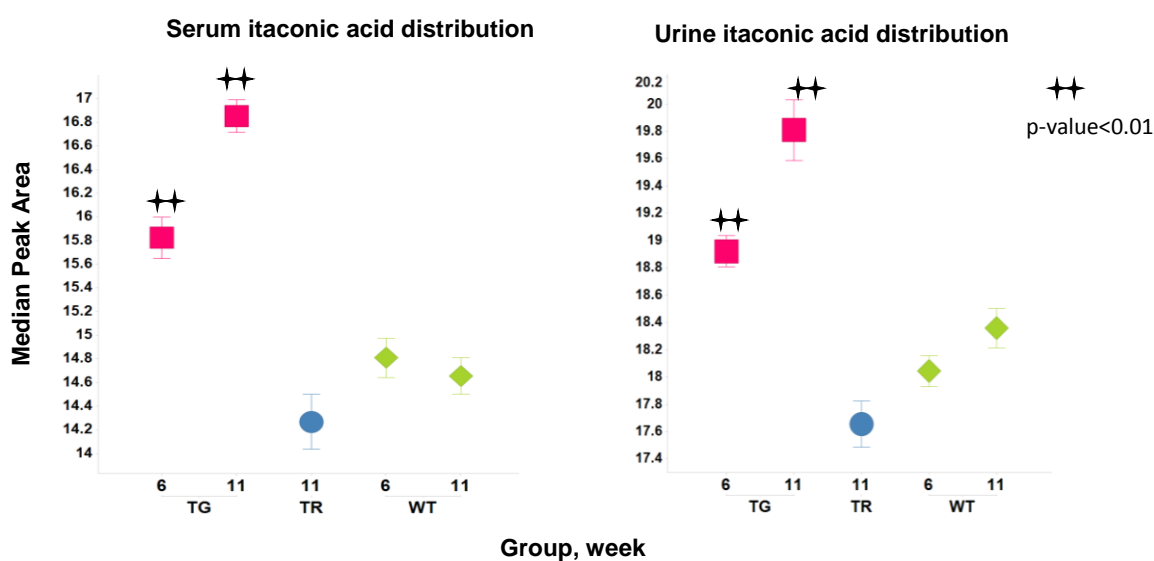


Figure S2: Itaconic acid median peak area distribution in serum and urine samples collected at week 6 and 11 of age. Vertical lines describe the standard error of the ion distribution at each group. ** p-values < 0.01 as calculated per group comparison to animals of the corresponding age from the healthy control group.

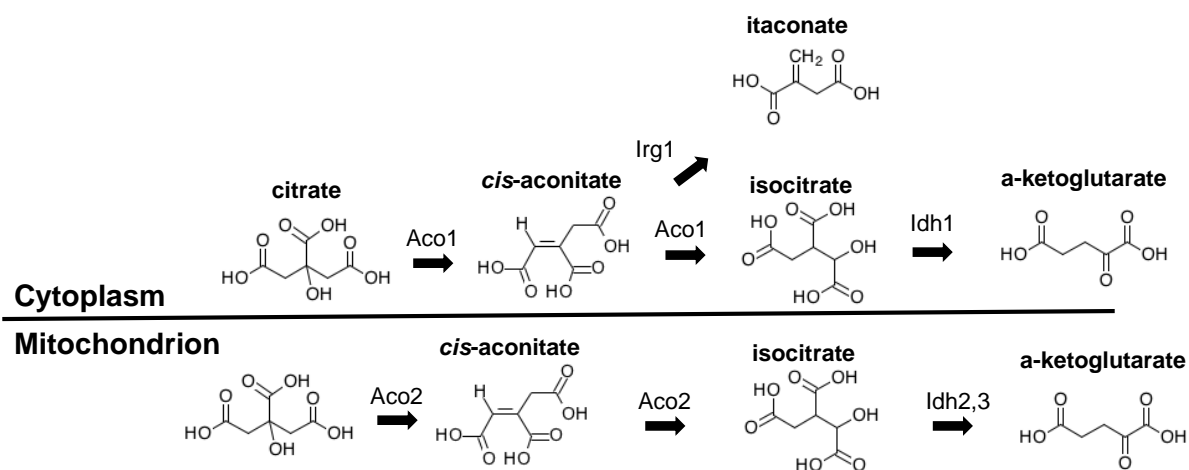


Figure S3: Detailed representation of citrate to a-ketoglutarate metabolism with associated enzymes located in the cytoplasm and mitochondrion.