

**Supplementary Table 1: Forward and reverse primers of the respective genes.**

<b>Gene</b>	<b>Forward primer 5'-3'</b>	<b>Reverse primer 5'-3'</b>
FTH1	CCGAGATGATGTGGCTCTGA	AGTCATCACGGTCTGGTTTCTTTA
TFRC	GAGCTATAAGCTTTGGGTGGGA	TGCTACAAGGGAGTACTAGGAAG
FPN1	GGTGGTTCAGAATGTGTCCGTCATC	GGATTGTGATCGCAGTGGCAGTAC
VEGF	TCCGTAGTAGCCGTGGTCTGC	CCCTCTCCTCTTCCTTCTCTTCCTC
SDF1	CATCGCCAGAGCCAACGTCAAG	AGCCGTGCAACAATCTGAAGGG
GPX4	GCCTGGATAAGTACAGGGGTT	CATGCAGATCGACTAGCTGAG
ACSL4	CTGATCTGCCTCCTGACGTTTGAA	ACAACGTCTTGCGTCTGAGAAGT
SLC7A11	TTGGAGCCCTGTCCTATGC	CGAGCAGTCCACCCAGAC
SLC3A2	GCAGGACGGTGTGGATGGTTTC	GCAGGTCGCTGGTGGATTCAAG
RPS29	GTCTGATCCGCAAATACGGG	AGCCTATGTCCTTCGCGTACT

**Abbreviations:**

FTH1: ferritin heavy chain 1, TFRC: transferrin receptor protein 1, FPN1: ferroportin-1, VEGF: vascular endothelial growth factor, SDF1: stromal cell-derived factor 1, GPX4: glutathione peroxidase 4, ACSL4: acyl-CoA synthetase long chain family member 4, SLC7A11: solute carrier family 7 member 11, SLC3A2: solute carrier family 3 member 2, RPS29: ribosomal protein S29

**Supplementary Table 2: Paw and ankle diameters (mm) shown as mean per cage on day 34.**

**A. Normal iron diet.**

	<b>LFP</b>	<b>RFP</b>	<b>LHP</b>	<b>RHP</b>	<b>LFA</b>	<b>RFA</b>	<b>LHA</b>	<b>RHA</b>
Round 1	1.64	1.50	2.22	1.87	1.84	1.63	2.11	1.86
Round 2	1.86	1.89	2.43	2.59	2.05	2.67	2.44	2.79
Round 3	2.11	2.48	2.56	2.46	2.43	2.84	2.96	2.66
Round 4	2.40	2.11	3.10	3.52	2.76	3.17	4.19	3.66
Round 6a	1.37	1.27	1.90	1.77	1.80	1.64	2.04	2.05
Round 6b	1.89	1.85	2.96	2.81	2.23	2.34	2.58	2.32

**B. Low iron diet.**

	<b>LFP</b>	<b>RFP</b>	<b>LHP</b>	<b>RHP</b>	<b>LFA</b>	<b>RFA</b>	<b>LHA</b>	<b>RHA</b>
Round 2	2.26	2.15	2.78	2.25	2.55	2.69	2.77	2.67
Round 3	2.65	2.82	2.95	2.78	2.98	3.05	2.78	3.33
Round 4	1.61	1.79	2.46	2.63	2.57	2.45	2.73	2.81
Round 6a	2.13	2.00	3.21	2.37	2.01	1.91	2.82	2.40
Round 6b	2.30	2.07	2.20	1.86	1.77	1.83	1.90	1.91

**Abbreviations:** LFP: left front paw, RFP: right front paw, LHP: left hind paw, RHP: right hind paw, LFA: left front ankle, RFA: right front ankle, LHA: left hind ankle, RHA: right hind ankle

**Supplementary Table 3: Weight development (g) during the experimental course shown as mean per cage.**

**A. Normal iron diet.**

	<b>Round 1</b>	<b>Round 2</b>	<b>Round 3</b>	<b>Round 4</b>	<b>Round 5</b>	<b>Round 6a</b>	<b>Round 6b</b>
<b>Day 0</b>	17.26	20.06	21.04		26.74	21.84	22.58
<b>Day 10</b>				26.88			
<b>Day 16</b>				26.38			
<b>Day 21</b>	18.68	22.24	21.98	26.24		24.00	22.94
<b>Day 24</b>						24.32	22.32
<b>Day 25</b>				26.38	26.00		
<b>Day 26</b>				25.94	25.20	23.76	22.32
<b>Day 27</b>				26.72	25.68		
<b>Day 28</b>				26.34	25.36	23.76	22.08
<b>Day 29</b>	18.76	21.44		26.10	25.06		
<b>Day 30</b>				25.58	25.20	23.80	22.16
<b>Day 31</b>	19.66		22.40	25.38	25.76		
<b>Day 32</b>				25.52	25.06	24.48	22.16
<b>Day 33</b>		21.44	22.28	26.10	25.04		
<b>Day 34</b>	19.66	21.12		25.48	24.96	24.74	22.48

**B. Low iron diet.**

	<b>Round 2</b>	<b>Round 3</b>	<b>Round 4</b>	<b>Round 5</b>	<b>Round 6a</b>	<b>Round 6b</b>
<b>Day 0</b>	21.06	21.64		25.65	23.82	22.28
<b>Day 8</b>			26.70			
<b>Day 10</b>						
<b>Day 16</b>			26.83			
<b>Day 21</b>	23.30	22.84	27.13		25.20	21.96
<b>Day 24</b>					25.78	21.74
<b>Day 25</b>			27.57	25.80		
<b>Day 26</b>			27.05	26.78	25.44	21.84
<b>Day 27</b>			27.50	26.73		
<b>Day 28</b>			26.98	26.90	25.42	21.74
<b>Day 29</b>	22.96		27.08	26.55		
<b>Day 30</b>			27.25	26.70	25.94	21.98

<b>Day 31</b>		23.18	26.93	25.83		
<b>Day 32</b>			26.55	25.35	25.28	22.04
<b>Day 33</b>	23.28		26.55	25.50		
<b>Day 34</b>	24.06	23.60	26.45	24.83	25.44	22.62

**Supplementary Table 4: Quantification of iron content (A), oxidative stress (B) and lipid peroxidation (C) in selected paws at day 34 from mice fed a normal iron diet or a low iron diet.**

**A.**

Normal iron diet			Low iron diet			
CAS	Fe <sup>2+</sup>	Fe <sup>3+</sup>	CAS	Fe <sup>2+</sup>	Fe <sup>3+</sup>	
1	30.85	14.09	1	66.62		Round 6a
0	51.06	7.05	1	23.27	6.12	
0	44.81	10.50	0	65.82	5.32	
1	64.62	1.86	1	44.14	17.82	
1	26.59	4.52	0	39.76	22.07	
0	28.19	4.92	0	25.40	10.24	Round 6b
0	44.28	5.05	1	34.17	8.51	
1	43.61		1	49.20	18.22	
1	69.41	7.85	1	22.74	6.38	
3	27.66	10.90	1	32.18	3.86	

Fe<sup>2+</sup> and Fe<sup>3+</sup> are depicted as µg per g tissue. **Abbreviations:** CAS: clinical arthritis score

**B.**

Normal iron diet				Low iron diet				
CAS	GSH	GSSG	GSH/GSSG (~ratio)	CAS	GSH	GSSG	GSH/GSSG (~ratio)	
1	0.55	0.98	0.56 (1:1.5)	1	0.41	1.43	0.29 (1:3)	Round 6a
0	0.63	1.29	0.49 (1:2)	1	0.54	1.22	0.44 (1:2.5)	
0	0.66	1.11	0.60 (1:1.5)	0	0.41	1.11	0.37 (1:2.5)	
1	1.01	1.05	0.96 (1:1)	1	0.74	0.99	0.75 (1:1.3)	
1	1.03	0.98	1.05 (1:1)	0	0.47	1.40	0.34 (1:3)	
0	0.73	1.28	0.57 (1:1.5)	0	0.44	1.28	0.34 (1:3)	Round 6b

0	0.14	0.71	0.20 (1:5)	1	0.57	1.22	0.47 (1:2)
1	1.09	1.12	0.97 (1:1)	1	0.91	1.28	0.71 (1:1.4)
1	0.74	1.12	0.66 (1:1.5)	1	0.22	1.51	0.15 (1:5)
3	0.62	1.31	0.47 (1:2)	1	1.22	1.17	1.04 (1:1)

GSH and GSSG are depicted as  $\mu\text{M}$  per g tissue. **Abbreviations:** CAS: clinical arthritis score, GSH: reduced glutathione, GSSG: oxidized glutathione

C.

Normal iron diet		Low iron diet		
CAS	MDA	CAS	MDA	
1	50.83	1	53.55	Round 6a
0	36.50	1	21.55	
0	137.16	0	30.16	
1	44.38	1	21.38	
1	66.16	0	25.22	
0	38.88	0	30.61	Round 6b
0	46.66	1	42.55	
1	44.77	1	77.00	
1	32.55	1	23.61	
3	13.44	1	42.88	

MDA is depicted as nmol per mg. **Abbreviations:** CAS: clinical arthritis score, MDA: malondialdehyde

**Supplementary Table 5: Relative gene expression of master regulator genes involved in (A) iron metabolism and (B) ferroptosis in selected paws at day 34 from mice under normal iron diet or low iron diet using the 2(-Delta C(T)) method.**

**A. Relative gene expression of FTH1, TFRC, FPN1, VEGF and SDF1**

Gene	Normal iron diet		Low iron diet	
	2(-Delta C(T))	CAS	2(-Delta C(T))	CAS
FTH1	<b>Round 4</b>		<b>Round 4</b>	
	0.052515	2	0.99274	1
	10.13349	2	2.022516	1
	3.646186	2	0.001084	1
	11.6005	2	11.7771	1
	0.135457	3		
	<b>Round 5</b>		<b>Round 5</b>	
	0.60039	1	4.280677	3
	0.906041	3	15.19163	1
	18.43435	1	0.298324	1
	0.036672	1	2.01016	1
	0.891844	2		
	<b>Round 6a</b>		<b>Round 6a</b>	
	113.4822	1	6.323192	3
	1.307808	2	5.445164	0
	0.075545	2	7.761434	0
	0.034889	0	0.098198	0
	0.182534	0	5.224502	0
	<b>Round 6b</b>		<b>Round 6b</b>	
	6.429885	2	0.006971	0
	0.366909	2	6.61629	0
	4.357648	3	1.122475	0
1.383708	1	0.179834	0	
0.984545	2	0.783455	0	
TFRC	<b>Round 4</b>		<b>Round 4</b>	
	9.515913	2	0.360692	1
	1.876179	2	1.023598	1
	7.759326	2	1.608761	1
	0.166692	3		
	<b>Round 5</b>		<b>Round 5</b>	
	0.47178	1	1.65812	3
	0.112945	3	4.324658	1
	4.988691	1	0.161552	1
	0.162908	2	1.453321	1
	<b>Round 6a</b>		<b>Round 6a</b>	
	2.160937	1	1.776302	3
	1.699111	2	0.582064	0
	0.161209	2	2.270829	0
	0.864524	0	0.171863	0
			1.968405	0
	<b>Round 6b</b>		<b>Round 6b</b>	
	5.757753	2	2.236388	0
1.000517	2	1.839951	0	

	1.51366	3	0.20819	0
	0.53528	1	1.469664	0
	0.41868	2		
FPN1	<b>Round 4</b>		<b>Round 4</b>	
	0.184884	2	0.440662	1
	3.057489	2	0.813413	1
	0.983298	2	0.245469	1
	6.118763	2	3.4771	1
	0.342052	3		
	<b>Round 5</b>		<b>Round 5</b>	
	1.279375	1	0.996979	3
	0.516985	3	5.695489	1
	8.141583	1	0.308699	1
	0.220468	1	1.864732	1
	0.724043	2		
	<b>Round 6a</b>		<b>Round 6a</b>	
	1.137336	1	2.934641	3
	1.224414	2	1.10364	0
	0.148329	2	2.852536	0
	1.019717	0	0.258135	0
	1.020624	0	1.418387	0
	<b>Round 6b</b>		<b>Round 6b</b>	
	4.145498	2	0.143329	0
	0.831311	2	6.052913	0
	3.991161	3	1.661272	0
	0.844824	1	0.174537	0
	0.40032	2	1.175216	0
VEGF	<b>Round 4</b>		<b>Round 4</b>	
	0.367676	2	0.796655	1
	1.864795	2	1.047319	1
	0.921281	2	0.064694	1
	4.061129	2	4.181434	1
	1.24903	3		
	<b>Round 5</b>		<b>Round 5</b>	
	0.498866	1	3.245595	3
	0.776395	3	2.56349	1
	2.892731	1	0.329721	1
	0.377394	1	1.615075	1
	0.73811	2		
	<b>Round 6a</b>		<b>Round 6a</b>	
	13.33958	1	1.684028	3
	1.701998	2	1.010347	0
	0.430776	2	1.570384	0
	0.482852	0	0.497295	0
	0.338412	0	1.733329	0
	<b>Round 6b</b>		<b>Round 6b</b>	
	1.544382	2	0.328002	0
	0.734112	2	2.229211	0
	1.114345	3	1.413787	0
	0.458773	1	0.362328	0
	1.079574	2	1.159217	0

SDF1	<b>Round 4</b>		<b>Round 4</b>	
	0.096265	2	0.682499	1
	4.961948	2	1.375416	1
	3.329794	2	0.037784	1
	4.171905	2	3.816341	1
	0.357934	3		
	<b>Round 5</b>		<b>Round 5</b>	
	0.87391	1	1.671161	3
	0.82371	3	4.164265	1
	3.074519	1	0.630369	1
	0.070702	1	1.684071	1
	2.690764	2		
	<b>Round 6a</b>		<b>Round 6a</b>	
	14.24845	1	8.799753	3
	0.874616	2	2.172325	0
	0.151171	2	3.150226	0
	0.340492	0	0.130634	0
	0.362174	0	1.661776	0
	<b>Round 6b</b>		<b>Round 6b</b>	
	10.2779	2	0.117085	0
	0.346007	2	5.749161	0
	8.017927	3	0.789001	0
	0.569126	1	0.356756	0
0.265254	2	0.40372	0	

#### Abbreviations:

CAS: clinical arthritis score, FTH1: ferritin heavy chain 1, TFRC: transferrin receptor protein 1, FPN1: ferroportin-1, VEGF: vascular endothelial growth factor, SDF1: stromal cell-derived factor 1

#### B. Relative gene expression of GPX4, ACSL4, SLC7A11 and SLC3A2

Gene	Normal iron diet		Low iron diet	
	2(-Delta C(T))	CAS	2(-Delta C(T))	CAS
GPX4	<b>Round 4</b>		<b>Round 4</b>	
	0.220572	2	1.184577	1
	5.515286	2	1.585844	1
	3.581581	2	0.028559	1
	6.089891	2	9.536992	1
	0.271714	3		
	<b>Round 5</b>		<b>Round 5</b>	
	1.215385	1	1.85961	3
	0.163006	3	13.04019	1
	8.283931	1	0.039897	1
	0.228675	1	2.020077	1
	0.369582	2		
	<b>Round 6a</b>		<b>Round 6a</b>	
	16.28695	1	1.537431	3
	2.241009	2	1.10543	0
	0.154659	2	3.973623	0

	0.25422	0	0.308296	0
	0.320202	0	2.192501	0
	<b>Round 6b</b>		<b>Round 6b</b>	
	1.922937	2	0.077761	0
	1.197464	2	4.331248	0
	1.913621	3	1.769526	0
	0.754269	1	0.240775	0
	0.654785	2	1.526637	0
ACSL4	<b>Round 4</b>		<b>Round 4</b>	
	11.13821	2	0.486835	1
	1.977995	2	1.848839	1
	3.598122	2	0.011157	1
	0.020038	3	4.619897	1
	<b>Round 5</b>		<b>Round 5</b>	
	0.617896	1	2.740061	3
	0.324042	3	8.848993	1
	9.165251	1	0.400129	1
	0.343061	2	2.221762	1
	<b>Round 6a</b>		<b>Round 6a</b>	
	17.67783	1	2.850439	3
	1.977793	2	0.774189	0
	0.121194	2	2.675425	0
	0.162572	0	0.05121	0
	0.037448	0	2.618581	0
	<b>Round 6b</b>		<b>Round 6b</b>	
	2.907228	2	3.600315	0
	1.33655	2	1.200128	0
	2.442841	3	0.252003	0
	9.291851	1	1.159994	0
	0.439521	2		
SLC7A11	<b>Round 4</b>		<b>Round 4</b>	
	1.198988	2	0.35655	1
	1.59073	2	2.232254	1
	0.863825	2	0.029347	1
	3.87783	2	4.223794	1
	4.050223	3		
	<b>Round 5</b>		<b>Round 5</b>	
	0.076879	1	1.709946	3
	0.92781	3	1.510964	1
	0.842451	1	0.368804	1
	0.755426	1	10.63743	1
	0.85132	2		
	<b>Round 6a</b>		<b>Round 6a</b>	
	94.3733	1	0.689447	3
	1.839551	2	0.514069	0
	0.338992	2	1.765991	0
	0.391821	0	0.434866	0
	0.118234	0	1.642179	0
	<b>Round 6b</b>		<b>Round 6b</b>	
	2.023809	2	0.656378	0
	0.353555	2	2.34996	0
	1.8436	3	1.757737	0

	0.228728	1	0.598017	0
	1.215641	2	1.379849	0
SLC3A2	<b>Round 4</b>		<b>Round 4</b>	
	0.020132	2	0.020104	1
	9.37878	2	0.441502	1
	2.888462	2	1.501537	1
	14.85697	2	7.392065	1
	0.257944	3		
	<b>Round 5</b>		<b>Round 5</b>	
	1.247842	1	0.110121	3
	0.769818	3	7.923386	1
	21.92408	1	24.75596	1
	0.021245	1	0.469907	1
	1.06934	2		
	<b>Round 6a</b>		<b>Round 6a</b>	
	26.37891	1	3.09952	3
	1.852454	2	1.120301	0
	0.14495	2	4.565421	0
	0.202767	0	0.135569	0
	0.279325	0	3.657822	0
	<b>Round 6b</b>		<b>Round 6b</b>	
	3.69618	2	0.048685	0
	0.773233	2	8.098519	0
	3.604028	3	1.310162	0
	0.669324	1	0.22408	0
	0.361561	2	1.098948	0

### Abbreviations

CAS: clinical arthritis score, GPX4: glutathione peroxidase 4, ACSL4: acyl-CoA synthetase long chain family member 4, SLC7A11: solute carrier family 7 member 11, SLC3A2: solute carrier family 3 member 2