

Supplementary Table S1. Composition of diets

Components	HFHSD	HFD	HSD	CD	HFHSD-M
Casein (%)	25.0	25.0	25.0	25.0	-
Soybean protein (%)	-	-	-	-	25.0
Cystine (%)	0.375	0.375	0.375	0.375	0.375
α -cornstarch (%)	14.9	34.9	9.87	14.9	14.9
β -cornstarch (%)	-	-	29.0	44.0	-
Sucrose (%)	20.0	-	20.0	-	20.0
Tallow (%)	14.0	14.0	2.00	2.00	14.0
Lard (%)	14.0	14.0	2.00	2.00	14.0
Soybean oil (%)	2.00	2.00	2.00	2.00	2
Cellulose powder (%)	5.00	5.00	5.00	5.00	5.00
AIN-93G mineral (%)	3.50	3.50	3.50	3.50	3.50
AIN-93G vitamin (%)	1.00	1.00	1.00	1.00	1.00
Choline bitartrate (%)	0.250	0.250	0.250	0.250	0.25
Tertiary butylhydroquinone (%)	0.0060	0.0060	0.0012	0.0012	0.0060
Total (%)	100	100	100	100	100
Total calories (kcal)	475.2	477.3	362.4	362.8	472.2

HFHSD: high fat high sucrose diet, HFD: high fat diet, HSD: high sucrose diet, CD: control diet, HFHSD-M: high fat high sucrose diet modified.

Supplementary Table S2. Cell blood counts on day7

	Mean±SD				p-value	
	Vehicle + NC	MTX + NC	Vehicle + HFHSD	MTX + HFHSD	MTX + HFHSD vs MTX + NC	MTX + HFHSD vs Vehicle + HFHSD
WBC (10 ² /μl)	63.0 ±10.4	88.3 ±15.5	65.0 ±20.0	30.5 ±16.7	0.021	0.043
RBC (10 ⁴ /μl)	1023 ±132	833 ±155	1112 ±46.1	1018 ±184	0.248	0.564
Hb (g/dL)	16.2 ±2.10	13.0 ±2.35	17.7 ±0.695	16.2 ±3.18	0.248	0.773
Ht (%)	48.7 ±5.82	39.9 ±7.40	53.3 ±1.98	47.6 ±8.22	0.248	0.564

Difference was tested by Mann-Whitney's U test (Mean±SD, n=5). MTX: methotrexate, NC: normal chow, HFHSD: high fat high sucrose diet, WBC: white blood cell, RBC: red blood cell, Hb: hemoglobin, Ht: hematocrit.

Supplementary Table S3. Metabolites with high absolute r values for the average relative survival period of each group.

	r	P
N-acetyl-L-glutamic acid	0.9695	0.0001
nicotinic acid	0.9487	0.0003
cholesterol sulfate	-0.9475	0.0003
L-glutamic acid	0.9444	0.0004
thiamine phosphate	0.9405	0.0005
β-alanine	0.9399	0.0005
L-malic acid	0.9366	0.0006
L-homoserine	0.9324	0.0007