Supplementary file

Biological pathways via which the anthocyanin malvidin alleviated the murine colitis induced by *Citrobacter rodentium*

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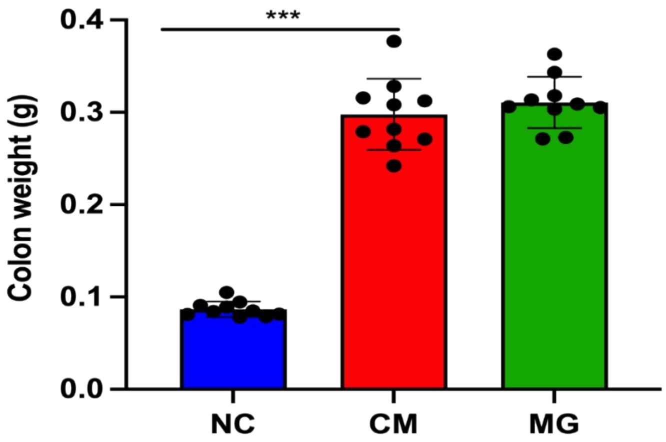
Figure S1. The colon weight (A) and the spleen index (the ratio of spleen weight to the total bodyweight) affected by *Citrobacter rodentium* infection and malvidin 3-glycoside supplementation in mice. NC: uninfected mice supplemented with PBS for 17 days. CM: *Citrobacter rodentium* infected mice supplemented with PBS for 17 days. MG: *Citrobacter rodentium* infected mice supplemented with malvidin 3-glycoside at 4.0 mg/kg bodyweight/day for a total of 17 days. * $p < 0.05$; *** $p < 0.001$.

A.



B.

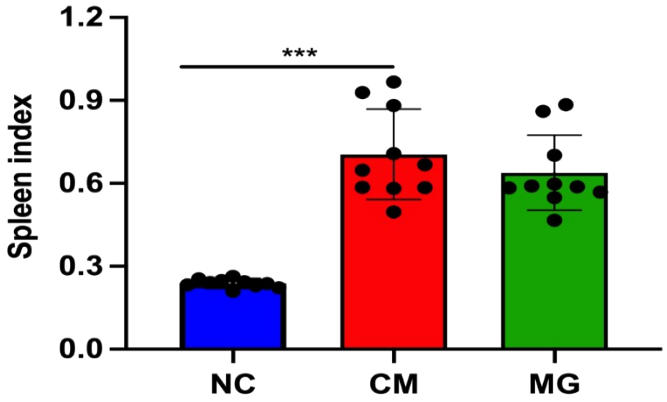


Figure S2. The colon histology score impacted by malvidin supplementation in mice infected by *Citrobacter rodentium*. CM: *Citrobacter rodentium* infected mice supplemented with PBS for 17 days. MG: *Citrobacter rodentium* infected mice supplemented with malvidin 3-glycoside at 4.0 mg/kg bodyweight/day for a total of 17 days.

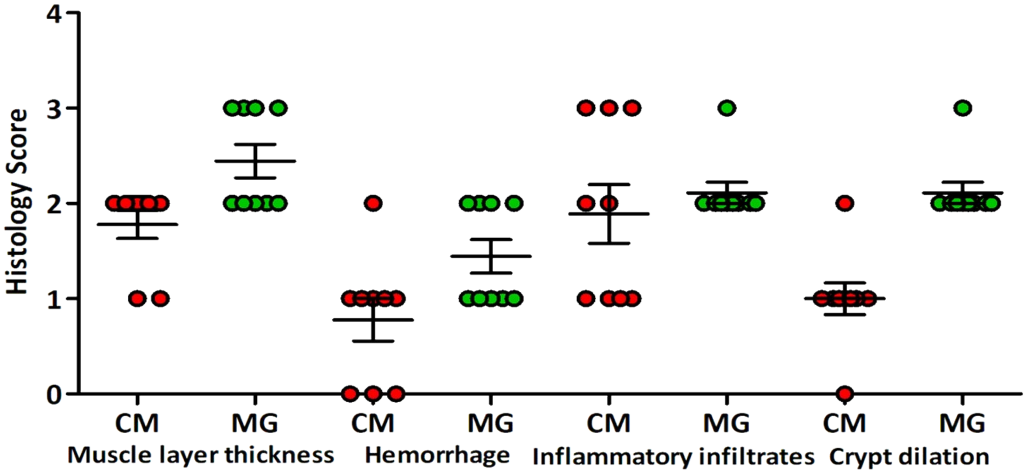


Figure S3. The colon transcriptome features, including genes and pathways, significantly regulated by *Citrobacter rodentium*. NC: uninfected mice supplemented with PBS for 17 days. CM: *Citrobacter rodentium* infected mice supplemented with PBS for 17 days. A: Volcano plot of RNAseq data. The $\log_2$ (FC) (fold change) is plotted on the x-axis, and the negative $\log_{10}$ *p*-value is plotted on the y-axis. B to F: Select pathways enriched among the genes significantly regulated in mice with by *Citrobacter rodentium* infection, compared to the uninfected control mice. NES: normalized enrichment score. FDR: false discovery rate.

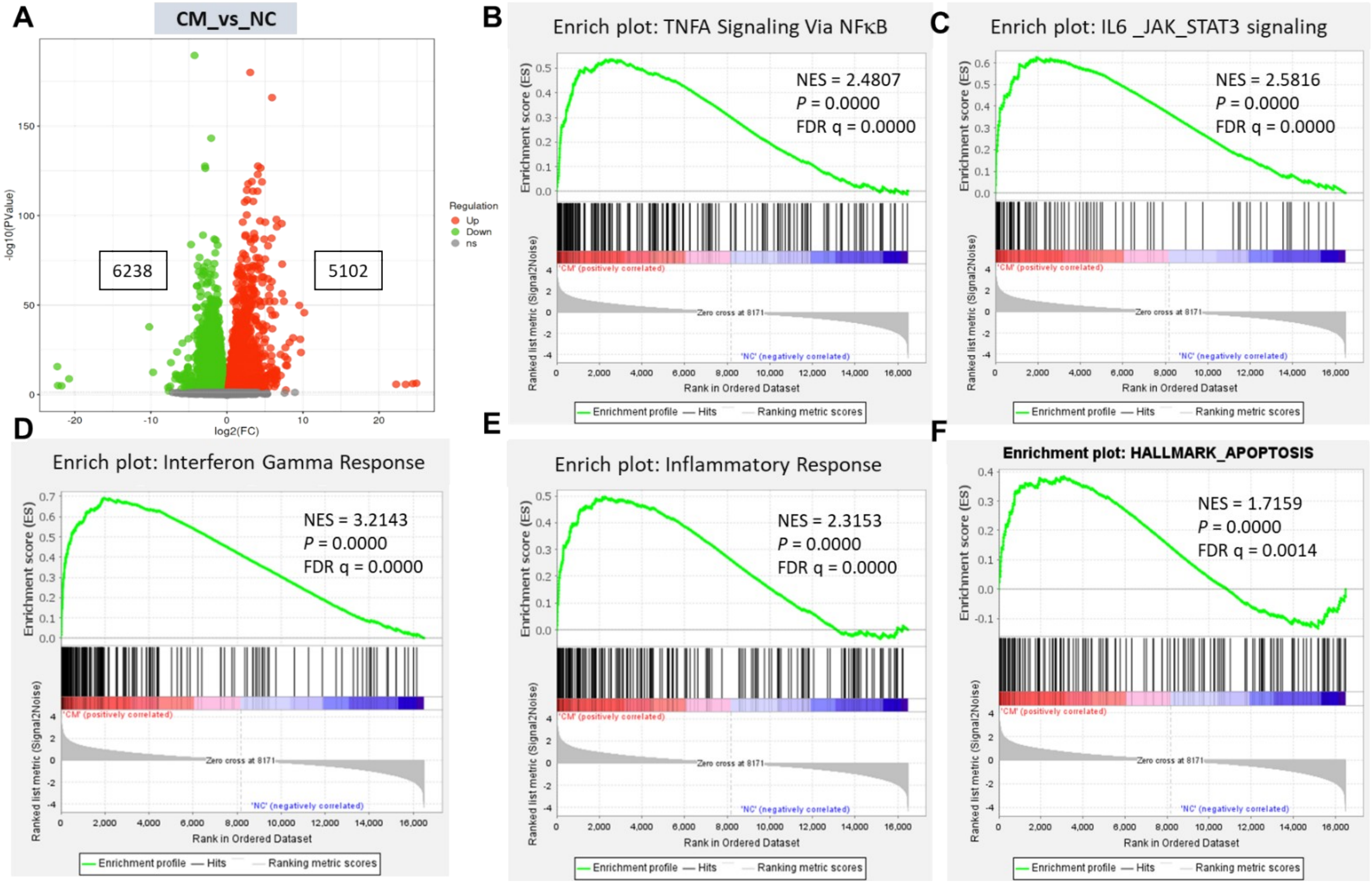


Figure S4. The origin of fecal metabolites predicted using MetOrigin. The origin of these metabolites includes those derived from either the host, or microbiota, or from both the host and microbiota (Co-metabolism) as well as others.

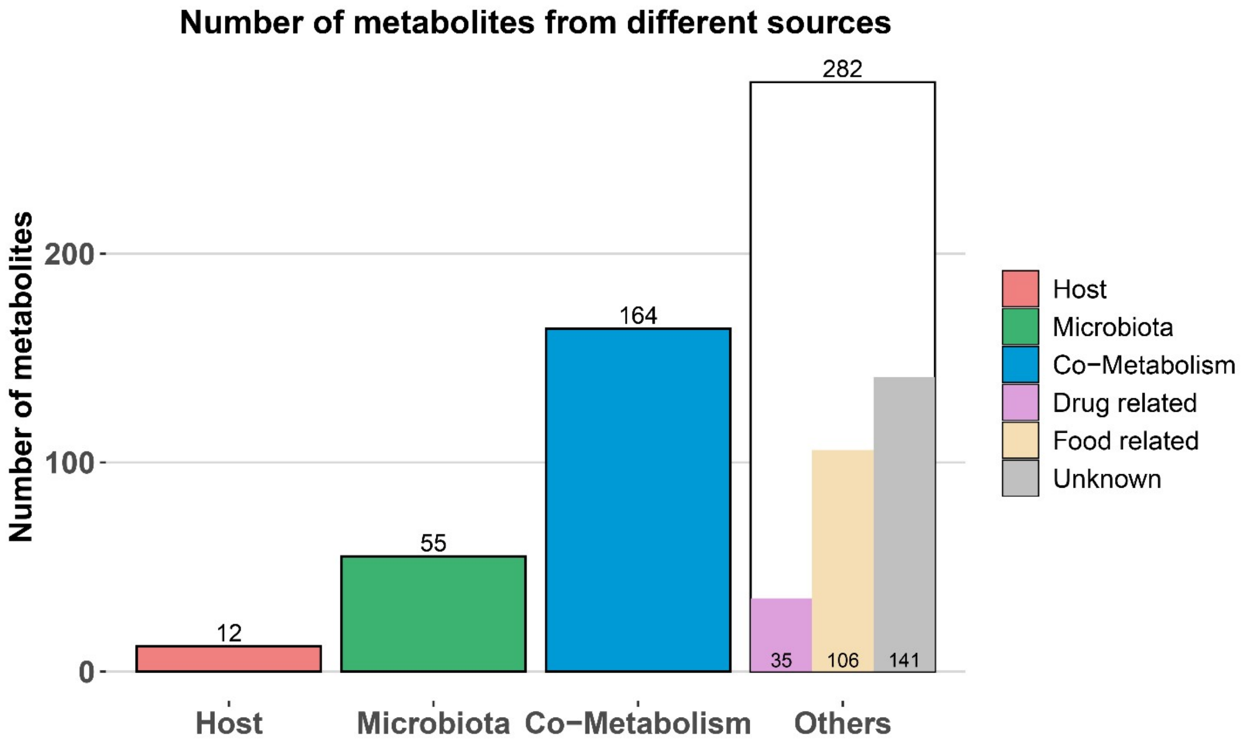


Table S1. The abundance of select bacterial species significantly changed by *Citrobacter rodentium* infection in mice. NC: uninfected mice supplemented with PBS for 17 days. CM: *Citrobacter rodentium* infected mice supplemented with PBS for 17 days. MG: *Citrobacter rodentium* infected mice supplemented with malvidin 3-glycoside at 4.0 mg/kg bodyweight/day for a total of 17 days. The number denotes the mean relative abundance ± SD.

Species	NC	CM	MG	LDA score	*P* value
Unassigned_Olsenella	0.0823 ± 0.1468	0.3506 ± 0.4108	0.1592 ± 0.1299	3.2080	0.0471
Alistipes finegoldii	0.0000 ± 0.0000	0.2979 ± 0.3353	0.1696 ± 0.1116	3.2985	0.0003
Lactobacillus vaginalis	0.0648 ± 0.1432	0.6825 ± 0.7836	0.2210 ± 0.2966	3.5585	0.0157
Clostridium perfringens	0.0018 ± 0.0057	2.6850 ± 3.9923	3.3158 ± 4.3089	4.2516	0.0072
Clostridium glycolicum	0.0000 ± 0.0000	0.2659 ± 0.2481	0.2011 ± 0.3160	3.2920	0.0003
Clostridium sordellii	0.0000 ± 0.0000	0.2676 ± 0.3978	1.1291 ± 1.2029	3.2925	0.0221
Unassigned_Anaerotruncus	0.3325 ± 0.2354	1.2694 ± 0.7069	1.0911 ± 0.5354	3.6914	0.0015
Clostridium cocleatum	1.4258 ± 0.9253	2.5707 ± 1.5494	2.5541 ± 0.9775	3.7121	0.0143
Unassigned_Sutterella	0.0000 ± 0.0000	1.6701 ± 1.6886	0.9985 ± 1.2407	3.9753	0.0003
Escherichia coli	0.1599 ± 0.5056	0.3158 ± 0.5300	0.0620 ± 0.1403	3.2423	0.0109
Citrobacter rodentium	0.0000 ± 0.0000	3.8477 ± 3.2648	7.9446 ± 9.6738	4.3423	0.0001
Unassigned_Coprococcus	0.7919 ± 0.4122	0.2006 ± 0.1939	0.3041 ± 0.3039	3.5621	0.0006
Ruminococcus gnavus	1.9307 ± 0.7485	1.1877 ± 0.6424	0.6436 ± 0.4298	3.5784	0.0222
Butyricicoccus pullicaecorum	0.0862 ± 0.0939	0.0193 ± 0.0578	0.0168 ± 0.0505	3.0663	0.0476
Unassigned_RF32	0.3607 ± 0.3110	0.0931 ± 0.2431	0.0751 ± 0.1536	3.2543	0.0198
Unassigned_Adlercreutzia	0.4919 ± 0.3032	0.1011 ± 0.1738	0.1477 ± 0.1661	3.4583	0.0044

Table S2. The fecal metabolites significantly dysregulated by *Citrobacter rodentium* infection and malvidin 3-glucoside supplementation. NC: uninfected mice supplemented with PBS for 17 days. CM: *Citrobacter rodentium* infected mice supplemented with PBS for 17 days. MG: *Citrobacter rodentium* infected mice supplemented with malvidin 3-glycoside at 4.0 mg/kg bodyweight/day for a total of 17 days. The number denotes the mean ion counts ± SD. The origin of metabolites was inferred using the MetOrigin algorithm.

Name	Origin	NC	CM	MG	Fold	*p* (NC vs CM)	*p* (CM vs MG)
N-Acetylputrescine	Co-Metabolism	1.1189 ± 1.4831	10.1703 ± 5.0177	6.314 ± 2.291	29.48	0.0023	
Squalene	Co-Metabolism	0.3889 ± 0.0647	4.1974 ± 1.6932	3.0676 ± 1.1509	9.96	0.0012	
Oleic acid	Co-Metabolism	4.8093 ± 4.9246	5.4285 ± 3.6158	5.341 ± 2.8399	7.18	0.0082	
Palmitoylcarnitine	Co-Metabolism	9.4341 ± 3.8369	65.7881 ± 20.4861	64.3342 ± 24.6927	6.64	0.0012	
Ceramide (d18:1/16:0)	Co-Metabolism	16.4381 ± 5.6982	236.5944 ± 394.8973	70.6582 ± 70.0082	5.01	0.0012	
LysoPC(18:1(9Z)/0:0)	Co-Metabolism	29.4715 ± 11.229	111.7864 ± 52.3429	94.2455 ± 55.1077	4.30	0.0023	
LysoPC(18:0/0:0)	Co-Metabolism	167.4379 ± 94.223	567.3946 ± 249.5765	382.2711 ± 191.5647	3.54	0.0047	
Formiminoglutamic acid	Co-Metabolism	12.8268 ± 10.9939	11.678 ± 6.1249	23.7389 ± 27.8749	3.49	0.0047	
Adenosine monophosphate	Co-Metabolism	0.9061 ± 0.3703	2.2868 ± 0.8307	2.1054 ± 1.0182	3.36	0.0082	
L-Proline	Co-Metabolism	6.2264 ± 2.7397	7.911 ± 2.8155	6.699 ± 2.288	2.95	0.0082	
Glycerol	Co-Metabolism	0.2344 ± 0.1885	0.9334 ± 0.8887	0.4237 ± 0.1513	2.88	0.0350	
Serotonin	Co-Metabolism	0.9959 ± 0.6129	2.1399 ± 0.4161	2.0793 ± 0.8743	2.48	0.0082	
N6,N6,N6-Trimethyl-L-lysine	Co-Metabolism	2.2164 ± 1.1474	5.046 ± 1.5498	4.7257 ± 0.9094	2.32	0.0082	
5-Hydroxy-L-tryptophan	Co-Metabolism	0.7597 ± 0.2983	1.5992 ± 0.5496	1.9882 ± 0.291	2.19	0.0221	
LysoPC(18:2(9Z,12Z)/0:0)	Co-Metabolism	4.2035 ± 1.6316	9.6513 ± 3.6322	8.0804 ± 3.6966	1.83	0.0023	
L-Alanine	Co-Metabolism	64.9977 ± 14.9276	92.2769 ± 22.4124	78.3869 ± 22.7049	1.44	0.0350	
Hypoxanthine	Co-Metabolism	250.3712 ± 49.3284	131.9108 ± 87.2681	221.9368 ± 138.3963	0.55	0.0082	
Estradiol	Co-Metabolism	1.9983 ± 0.3911	0.9276 ± 0.4978	0.6073 ± 0.2025	0.46	0.0023	
Ureidopropionic acid	Co-Metabolism	11.3101 ± 4.0908	4.3775 ± 1.6639	9.367 ± 3.3596	0.43	0.0012	0.0053
SM(d18:1/16:0)	Co-Metabolism	1.4144 ± 0.474	0.4179 ± 0.1633	2.2827 ± 0.6427	0.33	0.0012	0.0000
Bilirubin	Co-Metabolism	14.8996 ± 12.4967	6.6193 ± 6.0692	8.3942 ± 7.8876	0.33	0.0082	
Guanine	Co-Metabolism	3.1928 ± 3.0962	3.5521 ± 2.5029	3.0208 ± 2.1667	0.29	0.0023	

Cytidine	Co-Metabolism	3.3614 ± 2.1743	2.9756 ± 1.9853	3.7144 ± 2.8145	0.25	0.0012	
Indoleacetaldehyde	Co-Metabolism	3.2411 ± 1.4373	1.008 ± 0.7827	1.0281 ± 0.7333	0.22	0.0047	
Chenodeoxycholic acid	Co-Metabolism	1.5459 ± 0.6886	0.4676 ± 0.3377	0.7885 ± 0.8076	0.20	0.0221	
Adenine	Co-Metabolism	5.4195 ± 6.0782	11.1097 ± 10.4786	7.7146 ± 4.8749	0.12	0.0012	
Ibuprofen	Drug related	1.0995 ± 0.5975	0.2864 ± 0.3219	0.7337 ± 0.9815	0.17	0.0221	
LysoPE(18:1(9Z)/0:0)	Food related	7.9332 ± 2.4161	8.7991 ± 4.7369	7.8142 ± 2.3119	29.66	0.0012	
2-Nonenoic acid	Food related	0.199 ± 0.227	2.1135 ± 2.394	0.9652 ± 0.6797	9.86	0.0082	
Tridecanal	Food related	0.0656 ± 0.0753	0.7856 ± 0.9219	0.318 ± 0.22	9.66	0.0082	
6-Methyl-3,5-heptadien-2-one	Food related	0.3638 ± 0.3384	3.3425 ± 3.8205	1.5115 ± 0.9934	6.43	0.0140	
Methyl cyclohexanecarboxylate	Food related	0.1639 ± 0.1505	1.4918 ± 1.677	0.6983 ± 0.5174	5.81	0.0082	
LysoPC(0:0/16:0)	Food related	167.1232 ± 62.4088	639.3551 ± 163.9647	498.7405 ± 188.2891	4.47	0.0012	
N-Oleoylethanolamine (OEA)	Food related	1.2731 ± 0.2942	4.3487 ± 2.1688	2.0165 ± 0.7064	3.81	0.0012	0.0240
3-Methyl-2-cyclohexen-1-one	Food related	0.2882 ± 0.1773	2.1525 ± 2.43	0.9928 ± 0.7065	3.79	0.0082	
5,8,11-Eicosatrienoic acid	Food related	0.6155 ± 0.9148	1.5193 ± 1.7145	1.4741 ± 2.2441	3.69	0.0023	
gamma-Glutamylleucine	Food related	9.2415 ± 8.4199	6.9365 ± 6.1514	9.612 ± 5.8513	3.37	0.0082	
Docosapentaenoic acid (22n-3)	Food related	0.7005 ± 0.1144	2.8823 ± 1.6648	1.5558 ± 0.6563	3.13	0.0012	
Symmetric dimethylarginine	Food related	4.8073 ± 3.395	11.0121 ± 5.2605	7.7724 ± 0.9303	2.78	0.0350	
Aspartyllysine	Food related	3.3461 ± 1.1791	11.1456 ± 11.5649	10.5307 ± 4.3357	2.43	0.0350	
3-Aminobutanoic acid	Food related	7.1598 ± 2.8488	20.7883 ± 9.5392	18.5469 ± 16.7767	2.34	0.0023	
Adrenic acid	Food related	1.9822 ± 0.3305	5.0929 ± 1.7867	4.0495 ± 1.0047	2.21	0.0012	
LysoPE(0:0/18:3(6Z,9Z,12Z))	Food related	1.3082 ± 0.503	2.8693 ± 0.7328	2.4498 ± 0.5813	2.11	0.0023	
LysoPE(16:0/0:0)	Food related	209.1989 ± 136.5898	105.7962 ± 117.7473	221.1029 ± 120.5725	2.08	0.0012	
2,6-Di-tert-butylbenzoquinone	Food related	1.2268 ± 0.8981	0.3867 ± 0.138	0.4953 ± 0.222	0.46	0.0012	
2(R)-hydroxydocosanoic acid	Food related	12.8704 ± 8.7864	5.3895 ± 4.6386	22.6982 ± 11.3633	0.44	0.0221	0.0037
beta-Alanyl-L-lysine	Host	2.2592 ± 1.3749	5.3065 ± 1.7927	4.1126 ± 1.8815	3.17	0.0047	
Cytosine	Microbiota	67.9987 ± 16.8238	18.6541 ± 14.022	37.1268 ± 16.9667	0.20	0.0023	0.0395
4-Methylbenzaldehyde	Microbiota	37.6155 ± 31.4417	66.9417 ± 33.24	78.5327 ± 56.4077	2.32	0.0082	
Indolelactic acid	Microbiota	10.8099 ± 14.6424	21.8565 ± 14.4372	24.3267 ± 19.672	2.54	0.0221	
N-Acetylcadaverine	Microbiota	0.2934 ± 0.3723	2.1579 ± 0.9262	2.1132 ± 1.2653	15.87	0.0023	