

Figure S1 The IPA of potential biomarkers according to relative intensity analysis. A showed the most enriched pathways in the $APC^{min/+}$ mice. B manifested the prediction networks that associated with CRC in this study. The pathways (C) were ones related to the efficacy of mirabilite. And the network in D was a prediction network about the mechanism of action of mirabilite.

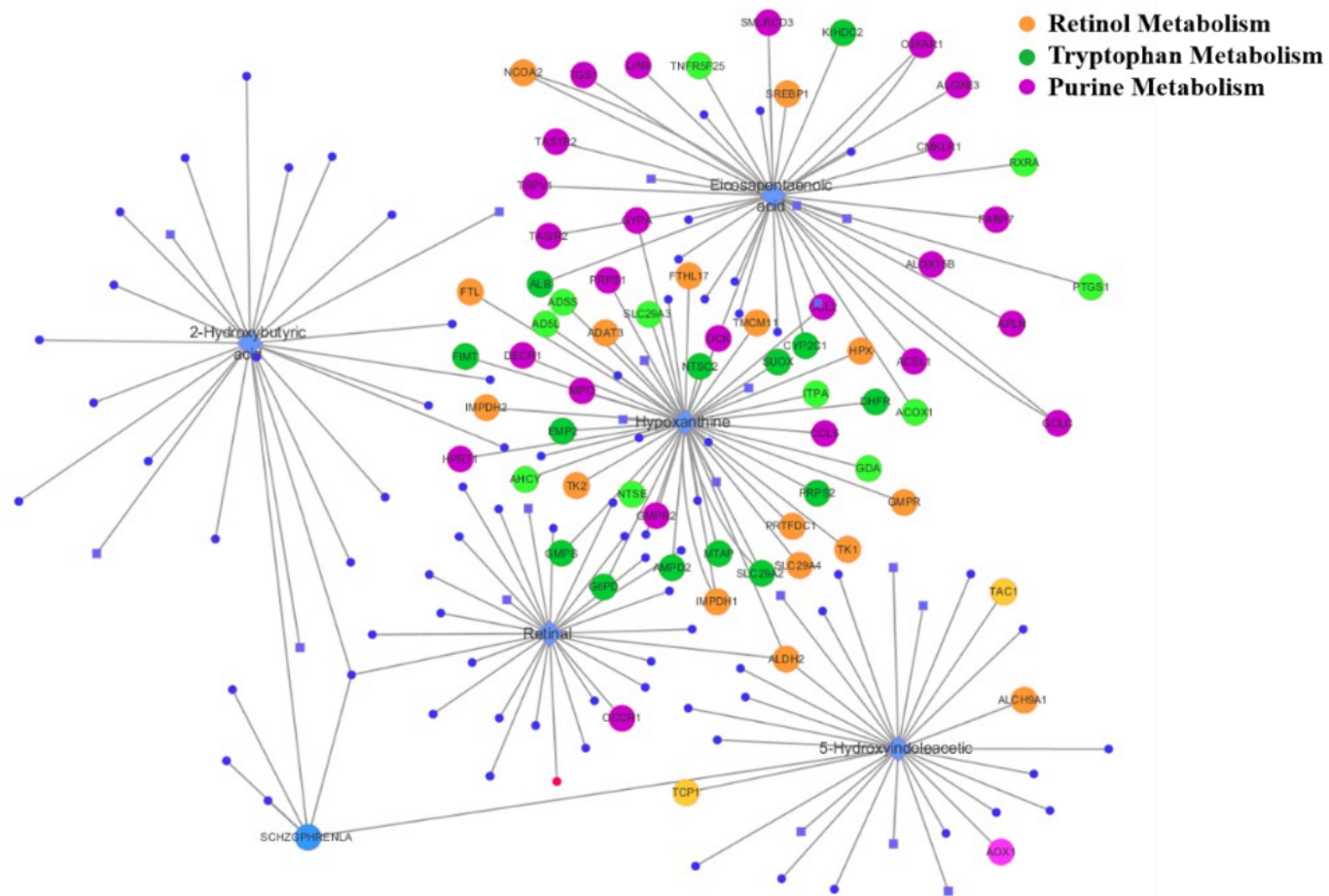


Figure S2 The network exploration of core metabolism by MetaboAnalyst 4.0.

The red, green, and purple circles represent genes associated with retinol acid metabolism, tryptophan metabolism, and purine metabolism, respectively.

Table S1 Potential biomarkers in the serum of CON, MOD and Mirabilite-treated mice

Index	Compounds	MS/MS fragment ion (m/z)	CON	MOD	Mirabilite
1	4-Aminobiphenyl	170.0970[M-C ₁₂ H ₁₂ N+H] ⁺ 92.0500[M-C ₆ H ₆ N+H] ⁺ 192.0661[M-C ₁₀ H ₁₀ NO ₃ +H] ⁺	219473.6±64056.1	140205.6±28025.2	124214.6±18597.0
2	5-Hydroxyindoleacetic acid	146.0606[M-C ₉ H ₈ NO+H] ⁺ 119.0497[M-C ₈ H ₇ O+H] ⁺ 137.0463[M+H] ⁺ 119.0358[M-C ₅ H ₃ N ₄ +H] ⁺	6598.2±1788.2	9844.9±1861.8	9962.3±1831.7
3	Hypoxanthine	111.0433[M-C ₄ H ₅ N ₃ O+H] ⁺ 94.0405[M-C ₄ H ₄ N ₃ +H] ⁺ 82.0405[M-C ₃ H ₄ N ₃ +H] ⁺ 67.0296[M-C ₃ H ₃ N ₂ +H] ⁺ 159.0684[M-C ₁₀ H ₉ NO+H] ⁺ 143.0735[M-C ₁₀ H ₉ N+H] ⁺	237277.4±1699.8	54983.3±32049.1	210672.5±66108.1
4	Indoleacetaldehyde	133.0653[M-C ₉ H ₉ O+H] ⁺ 130.0657[M-C ₉ H ₈ N+H] ⁺ 117.0578[M-C ₈ H ₇ N+H] ⁺ 105.0704[M-C ₈ H ₉ +H] ⁺	1680130.2±159679.0	2118058.0±212232.6	1811561.0±265189.3
5	L-Acetylcarnitine	146.0453[M-C ₅ H ₈ NO ₄ +H] ⁺ 119.0582[M-C ₅ H ₉ O+H] ⁺ 464.3141[M-C ₂₃ H ₄₇ NO ₆ P+H] ⁺	1327410.0±133772.1	1917996.4±213318.1	1252613.9±511906.7
6	LysoPC (15:0)	299.2586[M-C ₁₈ H ₃₅ O ₃ +H] ⁺ 166.0633[M-C ₅ H ₁₃ NO ₃ P+H] ⁺ 87.1048[M-C ₅ H ₁₃ N+H] ⁺	1364289.0±421351.7	2046426.6±306488.1	2943568.4±215280.1

7	LysoPC (16:1(9Z))	476.314[M-C ₂₄ H ₄₇ NO ₆ P+H] ⁺ 311.2586[M-C ₁₉ H ₃₅ O ₃ +H] ⁺ 258.102[M-C ₁₂ H ₁₉ O ₄ P+H] ⁺ 185.0814[M-C ₉ H ₁₃ O ₄ +H] ⁺ 166.0633[M-C ₅ H ₁₃ NO ₃ P+H] ⁺ 86.0970[M-C ₅ H ₁₂ N+H] ⁺	8810133.0±2502729.7	12351954.0±1076532.0	10510191.8±1109790.2
8	LysoPC (17:0)	492.3454[M-C ₂₅ H ₅₁ NO ₆ P+H] ⁺ 433.2719[M-C ₂₂ H ₄₂ O ₆ P+H] ⁺ 327.2899[M-C ₂₀ H ₃₉ O ₃ +H] ⁺ 185.0814[M-C ₉ H ₁₃ O ₄ +H] ⁺ 166.0633[M-C ₅ H ₁₃ NO ₃ P+H] ⁺ 87.1048[M-C ₅ H ₁₃ N+H] ⁺	594946.2±183986.3	928482.6±75309.5	1459741.2±129619.6
9	LysoPC (18:0)	341.3056[M-C ₂₁ H ₄₁ O ₃ +H] ⁺ 186.0892[M-C ₉ H ₁₄ O ₄ +H] ⁺ 86.0970[M-C ₅ H ₁₂ N+H] ⁺	137107.9±49814.4	216182.5±30099.7	180262.4±34408.6
10	LysoPC (18:1(9Z))	504.3454[M-C ₂₆ H ₅₁ NO ₆ P+H] ⁺ 185.0814 [M-C ₉ H ₁₃ O ₄ +H] ⁺ 125.0004[M-C ₂ H ₆ O ₄ P+H] ⁺ 86.0970[M-C ₅ H ₁₂ N+H] ⁺	73398318.0±49814.4	105965418.0±30099.6	134756860.0±34408.6
11	LysoPC (18:3(6Z,9Z,12Z))	335.2586[M-C ₂₁ H ₃₅ O ₃ +H] ⁺ 184.0736[M-C ₉ H ₁₂ O ₄ +H] ⁺ 166.0633[M-C ₅ H ₁₃ NO ₃ P+H] ⁺ 86.0970[M-C ₅ H ₁₂ N+H] ⁺	2153124.0±476753.1	2726491.8±265249.8	2725450.0±388029.0
12	LysoPC(18:4(6Z,9Z,12Z,15Z))	500.3141[M-C ₂₆ H ₄₇ NO ₆ P+H] ⁺ 459.2386[M-C ₂₂ H ₃₈ NO ₇ P+H] ⁺	280823.2±94306.5	430853.9±49376.6	377609.9±105188.4

		457.2355[M-C ₂₃ H ₃₈ O ₇ P+H] ⁺ 185.0814[M-C ₉ H ₁₃ O ₄ +H] ⁺ 146.9847[M-C ₄ H ₄ O ₄ P+H] ⁺ 125.0004[M-C ₂ H ₆ O ₄ P+H] ⁺ 86.0970[M-C ₅ H ₁₂ N+H] ⁺			
13	LysoPC (20:3(5Z,8Z,11Z))	489.2855[M-C ₂₄ H ₄₄ NO ₇ P+H] ⁺ 487.2825V[C ₂₅ H ₄₄ O ₇ P+H] ⁺ 146.9847[M-C ₄ H ₄ O ₄ P+H] ⁺	1017837.0±401249.0	1876566.4±303286.4	2167516.7±171787.3
14	LysoPC (20:4(5Z,8Z,11Z,14Z))	486.2621[M-C ₂₄ H ₄₁ NO ₇ P+H] ⁺ 184.0736[M-C ₉ H ₁₂ O ₄ +H] ⁺ 146.9847[M-C ₄ H ₄ O ₄ P+H] ⁺	2803618.0±947215.5	4002222.4±296092.6	3805189.8±318314.9
15	LysoPC (20:5(5Z,8Z,11Z,14Z,17Z))	524.3141[M-C ₂₈ H ₄₇ NO ₆ P+H] ⁺ 359.2586[M-C ₂₃ H ₃₅ O ₃ +H] ⁺ 285.2218[M-C ₂₀ H ₂₉ O+H] ⁺ 166.0633[M-C ₅ H ₁₃ NO ₃ P+H] ⁺ 86.0970[M-C ₅ H ₁₂ N+H] ⁺	140280.80±50864.8	298114.18±75689.2	228907.3±46201.7
16	LysoPC (P-18:1(9Z))	448.2828[M-C ₂₂ H ₄₃ NO ₆ P+H] ⁺ 181.0266[M-C ₅ H ₁₀ O ₅ P+H] ⁺ 163.0160[M-C ₅ H ₈ O ₄ P+H] ⁺ 86.0970[M-C ₅ H ₁₂ N+H] ⁺	247245.8±96590.7	475756.5±73994.7	665285.3±34345.7
17	Retinal	285.2218[M-C ₂₀ H ₂₉ O+H] ⁺ 241.1956[M-C ₁₈ H ₂₅ +H] ⁺ 211.1487[M-C ₁₆ H ₁₉ +H] ⁺ 145.1017[M-C ₁₁ H ₁₃ +H] ⁺ 14131.0861[M-C ₁₀ H ₁₁ +H] ⁺	377704.0±51049.4	496073.0±75288.8	368522.0±74337.8

18	Retinyl ester	303.2324[M-C ₂₀ H ₃₁ O ₂ +H] ⁺ 131.0861[M-C ₁₀ H ₁₁ +H] ⁺ 119.0861[M-C ₉ H ₁₁ +H] ⁺	3635709.0±79274.9	4902010.4±749247.3	3663042.10±699070.7
19	Uric acid	169.0362[M-C ₅ H ₅ N ₄ O ₃ +H] ⁺ 151.0256[M-C ₅ H ₃ N ₄ O ₂ +H] ⁺ 126.0304[M-C ₄ H ₄ N ₃ O ₂ +H] ⁺ 96.0198[M-C ₃ H ₂ N ₃ O+H] ⁺ 69.0089[M-C ₂ HN ₂ O+H] ⁺	997596.6±254464.0	1485024±388194.8	835745.3±466693.5
20	15(S)-HETE	119.0497[M--H] ⁻	7456424.0±1161624.9	9692761.0±1485045.5	13184068.0±1315254.9
21	2-Hydroxybutyric acid	103.04[M-H] ⁻	34815.1±6908.5	57588.8±12965.7	23034.7±18463.9
22	4-Pyridoxic acid	182.0453[M-H] ⁻ 156.0423[M--H] ⁻ 155.0582[M-C ₇ H ₉ NO ₃ -H] ⁻	31224.8±4096.6	22901.9±5510.6	20077.3±2140.1
23	6-Deoxocastasterone	450.3709[M-C ₂₈ H ₅₀ O ₄ -H] ⁻ 449.3631[M-C ₂₈ H ₄₉ O ₄ -H] ⁻ 431.3525[M-C ₂₈ H ₄₇ O ₃ -H] ⁻ 387.3627[M-C ₂₇ H ₄₇ O-H] ⁻	47312.6±28058.7	9074.9±7130.3	17370.8±8382.5
24	Eicosapentaenoic acid	283.2062[M-C ₂₀ H ₂₇ O-H] ⁻ 257.2269[M-C ₁₉ H ₂₉ -H] ⁻ 229.1956[M-C ₃ H ₄ O ₂ -H] ⁻ 175.1487[M-C ₁₃ H ₁₉ -H] ⁻	471430.4±78453.0	613586.1±88934.8	935282.2±87894.0
25	Linoleic acid	263.2375[M-C ₁₈ H ₃₁ O-H] ⁻	1746.5±758.2	819.9±302.1	1704.1±1290.9
26	LPA (0:0/16:0)	341.1882[M-C ₁₈ H ₃₀ O ₄ P-H] ⁻ 325.1780[M-C ₁₄ H ₃₀ O ₆ P-H] ⁻ 255.2324[M-C ₁₆ H ₃₁ O ₂ -H] ⁻	48305.6±23807.9	94187.7±23684.7	60220.7±13426.8

		171.0059[M-C ₃ H ₈ O ₆ P-H] ⁻			
		152.9953[M-C ₃ H ₆ O ₅ P-H] ⁻			
		78.9585[M-O ₃ P-H] ⁻			
		242.0794[M-C ₇ H ₁₇ NO ₆ P-H] ⁻			
27	LysoPC (16:0)	224.0688[M-C ₇ H ₁₅ NO ₅ P-H] ⁻	436486.5±162856.2	691035.0±63278.0	1024862.1±68239.0
		152.9953[M-C ₃ H ₆ O ₅ P-H] ⁻			
		78.9585[M-O ₃ P-H] ⁻			
28	Stearic acid	265.2531[M-C ₁₈ H ₃₃ O-H] ⁻	168738.8±53758.8	261246.2±57217.3	323997.3±17676.1

Table S2 Relative pathways and enzymes of biomarkers in APC^{min/+} mice

Biomarkers	Pathways	Enzymes
4-Pyridoxic acid	map00750 Vitamin B6 metabolism	1.2.3.1 aldehyde oxidase
	map01100 Metabolic pathways	1.2.3.8 pyridoxal oxidase
	map01120 Microbial metabolism in diverse environments	3.1.1.27 4-pyridoxolactonase
5-Hydroxyindoleacetic acid	map00380 Tryptophan metabolism	1.2.1.3 aldehyde dehydrogenase (NAD ⁺)
		1.2.3.1 aldehyde oxidase
		2.1.1.4 acetylserotonin O-methyltransferase
6-Deoxocastasterone	map00905 Brassinosteroid biosynthesis	1.14.-.-
	map01100 Metabolic pathways	
	map01110 Biosynthesis of secondary metabolites	
Eicosapentaenoic acid	map01040 Biosynthesis of unsaturated fatty acids	3.1.2.2 palmitoyl-CoA hydrolase 5.3.3.13 polyenoic fatty acid isomerase
Hypoxanthine	map00230 Purine metabolism	1.17.1.4 xanthine dehydrogenase
	map01100 Metabolic pathways	1.17.3.2 xanthine oxidase
		2.4.2.1 purine-nucleoside phosphorylase
		2.4.2.4 thymidine phosphorylase
		2.4.2.8 hypoxanthine phosphoribosyltransferase
		2.4.2.15 guanosine phosphorylase
		2.4.2.44 S-methyl-5'-thioinosine phosphorylase ₃
		.2.2.1 purine nucleosidase
		3.2.2.2 inosine nucleosidase
		3.2.2.12 inosinate nucleosidase
		3.2.2.26 fufalosine hydrolase
		3.5.4.2 adenine deaminase
	L-Acetylcarnitine	map04931 Insulin resistance

Linoleic acid	map00591	Linoleic acid metabolism	1.13.11.12	acyl-lipid Delta12-acetylenase
	map01040	Biosynthesis of unsaturated fatty acids	1.13.11.33	arachidonate 15-lipoxygenase
			1.13.11.45	linoleate 11-lipoxygenase
	map01060	Biosynthesis of plant secondary metabolites	1.13.11.58	linoleate 9S-lipoxygenase
			1.13.11.60	linoleate 8R-lipoxygenase
	map01100	Metabolic pathways	1.13.11.62	linoleate 10R-lipoxygenase
			1.13.11.77	oleate 10S-lipoxygenase
			1.14.14.1	unspecific monooxygenase
			1.14.19.3	acyl-CoA 6-desaturase
			1.14.19.39	acyl-lipid Delta12-acetylenase
LysoPC(20:5(5Z,8Z,11Z,14Z,17Z))	map00564	Glycerophospholipid metabolism	2.3.1.23	L-acylglycerophosphocholine O-acyltransferase
	map05231	Choline metabolism in cancer	2.3.1.43	phosphatidylcholine-sterol O-acyltransferase
			2.3.1.83	phosphatidylcholine-dolichol O-acyltransferase
			3.1.1.4	phospholipase A
			3.1.2.2	palmitoyl-CoA hydrolase
			5.2.1.5	linoleate isomerase
			3.1.1.4	phospholipase A2
			3.1.1.5	lysophospholipase
			5.4.1.1	lysolecithinacylmutase
	Retinal	map00830	Retinol metabolism	1.1.1.1
map01100		Metabolic pathways	1.1.1.105	all-trans-retinol dehydrogenase (NAD ⁺)
map04744		Phototransduction	1.1.1.300	NADP-retinol dehydrogenase
map04977		Vitamin digestion and absorption	1.2.1.36	retinal dehydrogenase
			1.2.3.1	aldehyde oxidase
			1.13.11.63	beta-carotene 15,15'-dioxygenase
			1.13.11.75	all-trans-8'-apo-beta-carotenal 15,15'-oxygenase
Retinyl ester	map00830	Retinol metabolism	2.3.1.76	retinol O-fatty-acyltransferase
	map04977	Vitamin digestion and absorption	2.3.1.135	phosphatidylcholine-retinol O-acyltransferase
			3.1.1.64	retinoid isomerohydrolase
			3.1.1.90	all-trans-retinyl ester 13-cis isomerohydrolase

Stearic acid	map00061	Fatty acid biosynthesis	3.1.2.2	palmitoyl-CoA hydrolase		
	map01040	Biosynthesis of unsaturated fatty acids	3.1.2.14	oleoyl-[acyl-carrier-protein] hydrolase		
	map01060	Biosynthesis of plant secondary metabolites				
	map04745	Phototransduction - fly				
Uric acid	map00230	Purine metabolism	1.7.3.3	factor-independent	urate	
	map01100	Metabolic pathways		hydroxylase		
	map01120	Microbial metabolism in diverse environments	1.14.11.48	xanthine dioxygenase		
	map04976	Bile secretion		1.14.13.113	FAD-dependent	urate
					hydroxylase	
					1.17.1.4	xanthine dehydrogenase
				1.17.3.2	xanthine oxidase	
		2.4.2.16	urate-ribonucleotide phosphorylase			
		3.5.4.32	8-oxoguanine deaminase			
