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### **Supplemental Material**

#### ***In Vivo* Tissue Distribution of Polystyrene or Mixed Polymer Microspheres and Metabolomic Analysis after Oral Exposure in Mice**

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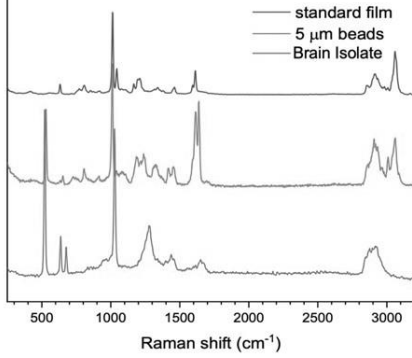
**Table S13.** Targeted Metabolomics of Colon in Mice Exposed to Polystyrene showing significantly altered metabolites for concentrations A) 2mg/week and B) 4mg/week.

**Table S14.** Targeted Metabolomics of Colon in Mice Exposed to Mixed Polymer showing significantly altered metabolites for concentrations A) 2mg/week and B) 4mg/week.

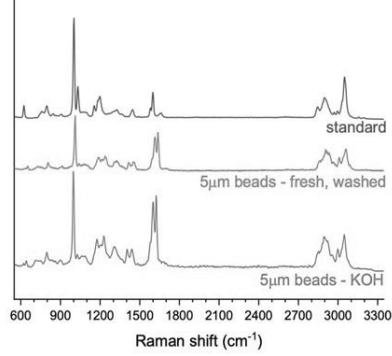
**Additional File-** Excel Document

**Figure S1.**

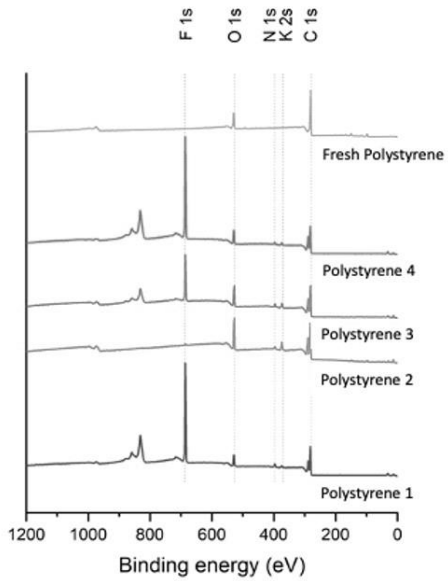
**A. Raman Data - Brain**



**B. Raman Data – PS KOH**



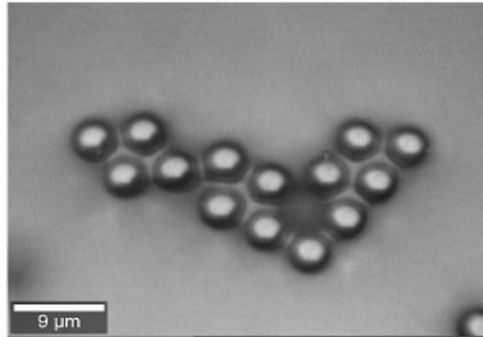
**C. XPS Data - PS**



**D. Elemental Expression - PS**

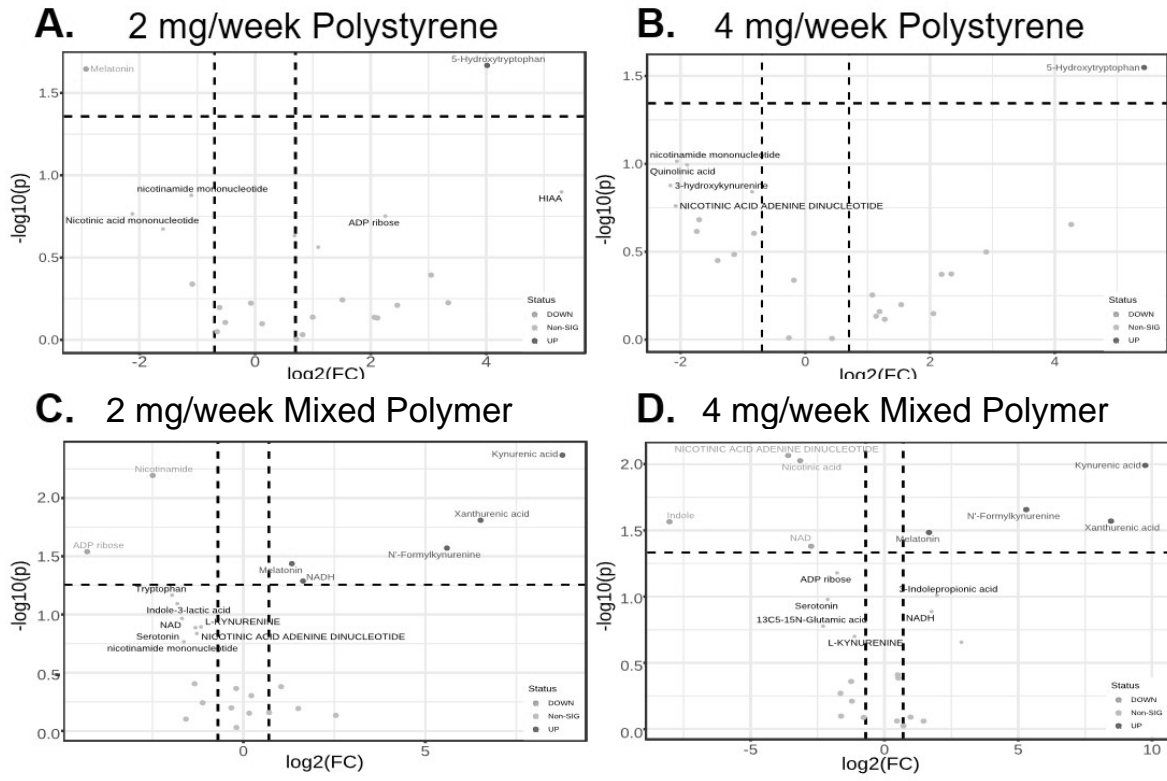
Liver Polystyrene Exposure	C 1s%	F 1s%	K 1s%	N 1s%	O 1s%
Polystyrene 1	54.21	34.30	2.31	2.79	6.39
Polystyrene 2	75.02	0.83	8.48	2.20	13.48
Polystyrene 3	64.05	19.22	5.08	2.34	9.30
Polystyrene 4	55.10	32.72	3.11	1.83	7.23
Fresh Polystyrene (non-exposed)	85.40	0.00	0.00	0.46	14.14

**E. Fresh PS**



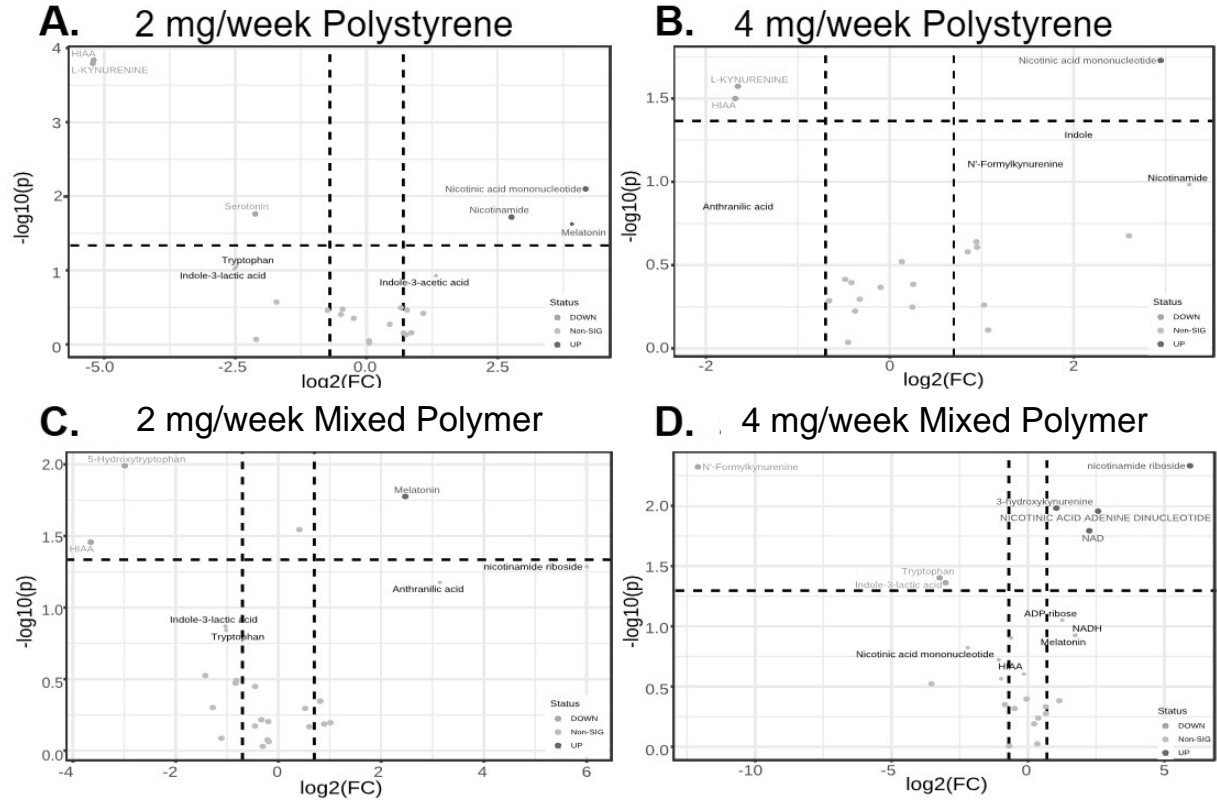
**Figure S1. Raman Spectroscopy in the liver.** A) Raman spectra of polystyrene microspheres isolated from brain isolates compared to fresh 5  $\mu\text{m}$  polystyrene microspheres and standard library film polystyrene. Brain tissue was isolated from mice exposed twice a week for 4 weeks to 2 or 4 mg 5  $\mu\text{m}$  polystyrene microspheres. B) Raman Spectroscopy of 5  $\mu\text{m}$  polystyrene microspheres exposed to potassium hydroxide (KOH) digestion compared to fresh 5  $\mu\text{m}$  polystyrene microspheres and standard library film polystyrene. C) XPS data comparing 4 representative polystyrene microspheres isolated from the liver of mice exposed twice a week for 4 weeks via oral gavage to fresh polystyrene microspheres at both 2mg/week and 4mg/week exposure groups. Polystyrene 1 and Polystyrene 2 were representative of mice exposed to polystyrene at the 2mg/week dose. Polystyrene 3 and Polystyrene 4 were representative of mice exposed to polystyrene at the 4mg/week. D) Elemental expression of each polystyrene sample isolated from the liver of exposed mice compared to fresh polystyrene microspheres. E) Visualization of fresh polystyrene microspheres used for XPS Analysis (60x magnification).

Figure S2.



**Figure S2. Targeted metabolomics in colon.** Volcano plots of targeted metabolomic analysis in the colon of mice exposed to A) 2 mg/week polystyrene (5  $\mu\text{m}$ ), B) 4 mg/week polystyrene, C) 2 mg/week mixed polymer (5  $\mu\text{m}$ ), and D) 4 mg/week mixed polymer. Exposures were four weeks in duration twice weekly via oral gavage. Mixed polymer: polystyrene, polyethylene, and poly-(lactic-co-glycolic acid) microspheres. Exposure groups were compared to 0 mg/week controls. Data are plotted as log(2) fold change ( $p < 0.05$ ;  $n=8$  per group). Summary data can be found in Excel Tables S3 and S4.

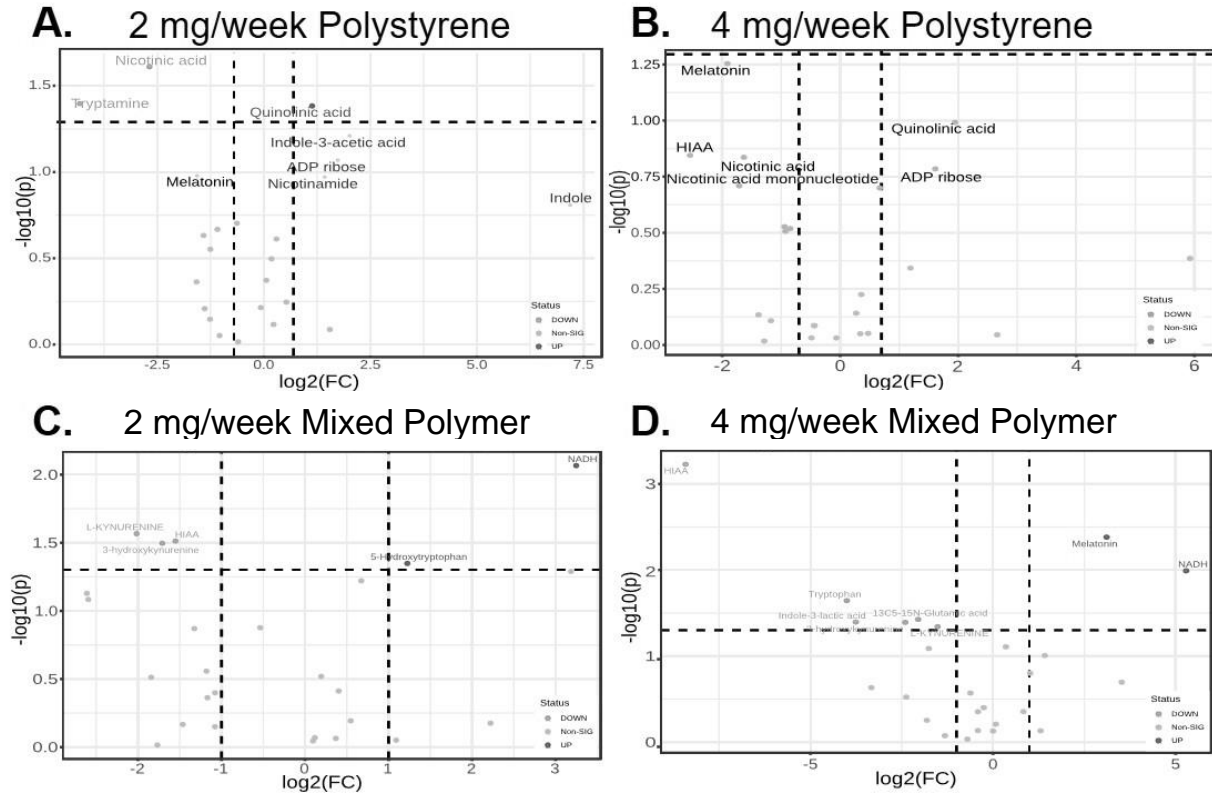
Figure S3.



**Figure S3. Targeted metabolomics in liver.** Volcano plots showing targeted metabolomic analysis of livers from mice exposed to A) 2 mg/week polystyrene, B) 4 mg/week polystyrene C) 2 mg/week mixed polymer, or D) 4 mg/week mixed polymer. Exposures were four weeks in duration twice weekly via oral gavage. Mixed polymer: polystyrene, polyethylene, and poly-(lactic-co-glycolic acid) microspheres. Exposure groups were compared to 0 mg/week controls. Data are plotted as log<sub>2</sub> fold change (p < 0.05; n=8 per group). Summary data can be found in Excel Tables S7 and S8.



Figure S4.



**Figure S4. Targeted metabolomics in brain.** Volcano plots showing targeted metabolomic analysis of brain isolates from mice exposed to A) 2 mg/week polystyrene, B) 4 mg/week polystyrene C) 2 mg/week mixed polymer, or D) 4 mg/week mixed polymer. Exposures were four weeks in duration twice weekly via oral gavage. Mixed polymer consisted of polystyrene, polyethylene, and poly-(lactic-co-glycolic acid) microspheres. Exposure groups were compared to 0 mg/week controls. Data are plotted as log(2) fold change ( $p < 0.05$ ;  $n=8$  per group). Summary data can be found in Excel Tables S11 and S12.

Tables S1 through S12 are also available in the supplemental Excel file as Excel Tables S15 through S27.

**Table S1.**

Untargeted Metabolomic Analysis in Colon Tissue of Mice Exposed to Polystyrene (2mg/week) p = 0.05	FC	log2(FC)	raw.pval	-LOG10(p)
<b>Lower</b>				
hexahydro-2-oxo-1h-thieno(3,4-d)imidazole-4-pentanoic acid	0.043836	-4.5117	0.00028512	3.545
Homocarnosine	0.05326	-4.2308	0.00581	2.2358
2-(Acetylsulfamoyl)benzoic acid	0.085277	-3.5517	0.0067949	2.1678
n-Hexanamide	0.093022	-3.4263	0.003858	2.4136
Carnosine	0.095824	-3.3835	0.00049343	3.3068
2-Mercapto-3-methylbutan-1-ol	0.098894	-3.338	0.00618	2.209
4-Hydroxy-4-(methylnitrosoamino)-1-(3-pyridinyl)-1-butanone	0.09993	-3.3229	0.00501	2.3002
2-[(7-methyl-2,3-dihydro-1H-inden-4-yl)oxy]pyridin-3-amine	0.09993	-3.3229	0.00501	2.3002
Zalcitabine	0.10351	-3.2722	0.0065762	2.182
MFCD12546417	0.11344	-3.14	0.023667	1.6259
EIPA	0.11351	-3.1392	0.0034265	2.4652
3-Hydroxysebacic acid	0.13861	-2.8509	0.0024408	2.6125
N-[(1S,3aS,5S,7aR)-7a-{3-[(2-Furylmethyl)amino]-3-oxopropyl}-5-hydroxy-3,3,5-trimethyloctahydro-1H-inden-1-yl]benzamide	0.14429	-2.7929	0.0087096	2.06
4-phenolsulfonic acid	0.19723	-2.342	0.028575	1.544
Clavam-2-carboxylate	0.20186	-2.3085	0.022086	1.6559
(1S,6S)-6-Aminooctahydro-1-indoliziny acetate	0.21514	-2.2167	0.0062974	2.2008
Rhodamine 6G	0.22321	-2.1636	0.016971	1.7703
THTA	0.22822	-2.1315	0.021597	1.6656
5-Butyloxazole	0.236	-2.0831	0.04328	1.3637
N-Acetyl-L-leucine	0.24101	-2.0529	0.032579	1.4871
Helicid	0.24377	-2.0364	0.023885	1.6219
n-Amylbenzene	0.26717	-1.9042	0.015652	1.8054
Drotaverine	0.27506	-1.8622	0.0061502	2.2111
2-Methyl-3-phenylpropyl hydrogen sulfate	0.29297	-1.7712	0.018204	1.7398
2-Methyl-3-hydroxybutyric acid	0.29373	-1.7674	0.016305	1.7877
3-Sulfamoylalanine	0.31185	-1.6811	0.021678	1.664
RG5927903	0.31272	-1.6771	0.022334	1.651
DA6495000	0.31584	-1.6627	0.016139	1.7921
asn-lys	0.32104	-1.6392	0.021943	1.6587
indospicine	0.32411	-1.6255	0.027743	1.5569

1-(sn-glycero-3-phospho)-1D-myo-inositol	0.32962	-1.6011	0.0048315	2.3159
3-Deoxy-D-manno-octulosonic acid	0.33263	-1.588	0.025716	1.5898
Methylimidazoleacetic acid	0.34119	-1.5514	0.015784	1.8018
6-Acetamido-2-oxohexanoic acid	0.34364	-1.541	0.035644	1.448
Droxidopa	0.35512	-1.4936	0.027794	1.5561
(2S)-2-Piperazinecarboxylic acid	0.35735	-1.4846	0.041127	1.3859
2-Oxobutyric acid	0.35892	-1.4783	0.025763	1.589
Glycine	0.36283	-1.4626	0.016051	1.7945
clavulanic acid	0.37028	-1.4333	0.027849	1.5552
1H-Imidazol-2-ol	0.40679	-1.2977	0.0010453	2.9808
GLY-MET	0.41664	-1.2631	0.034937	1.4567
(S)-(+)-allantoin	0.41891	-1.2553	0.042623	1.3704
methocarbamol	0.42813	-1.2239	0.0081159	2.0907
Pimnidazole	0.43457	-1.2023	0.0077735	2.1094
3,4-Dehydroproline	0.43781	-1.1916	0.011137	1.9532
3-Oxotetradecanoic acid	0.43803	-1.1909	0.0010096	2.9959
(S)-(+)-2-Amino-1-propanol	0.45124	-1.148	0.032261	1.4913
Propionylcarnitine	0.45158	-1.1469	0.0011722	2.931
(1S,2R,5S)-2-Isopropyl-5-methylcyclohexyl 3-oxobutanoate	0.46424	-1.107	0.00096884	3.0137
1-Methylhistidine	0.47362	-1.0782	0.0036394	2.439
{[5-[(2S)-2-Carboxy-2-(trimethylammonio)ethyl]-1H-imidazol-2-yl]sulfanyl}oxidanide	0.47626	-1.0702	0.04364	1.3601
2-methylbutyrylcarnitine	0.4798	-1.0595	0.032007	1.4948
streptidine	0.48833	-1.0341	0.019481	1.7104
[Similar to: 2-benzylideneindan-1-one; _Mass: 165.0170 Da]	0.49117	-1.0257	0.038758	1.4116
(3S)-3-(Pentanoyloxy)-4-(trimethylammonio)butanoate	0.49545	-1.0132	0.030221	1.5197
(11Z)-eicoseneoylcarnitine	0.49803	-1.0057	0.0033106	2.4801
Traumatin	0.49983	-1.0005	0.033616	1.4735
<b>Higher</b>				
4-styrylpyridine	2.0216	1.0155	0.026322	1.5797
_Estradiol-17_-glucuronide	2.0716	1.0508	0.04306	1.3659
dacisteine	2.2486	1.169	0.026331	1.5795
(5S,9R)-12-[(2R)-6-Hydroxy-2,5,7,8-tetramethyl-3,4-dihydro-2H-chromen-2-yl]-5,9-dimethyldodecanoic acid	2.2495	1.1696	0.026592	1.5752
(+)-ar-Turmerone	2.2648	1.1794	0.016288	1.7881
5(6)-EET Ethanolamide	2.3496	1.2324	0.011287	1.9474
4-amino-2-hydroxyamino-6-nitrotoluene	2.362	1.24	0.015436	1.8115
(2S,3S)-2,3-dihydro-3-hydroxyanthranilic acid zwitterion	2.4954	1.3193	0.01854	1.7319
RPI-1	2.9104	1.5412	0.039482	1.4036
Crotanecine	2.9162	1.5441	0.02966	1.5278

N-(Carboxymethyl)norleucine	3.0728	1.6195	0.037301	1.4283
(2E)-3-Cyano-2-methyl-2-propen-1-yl stearate	3.0751	1.6206	0.0053356	2.2728
Elatine	3.2617	1.7056	0.015596	1.807
3-(2,6-dichlorophenyl)-N-(1,4-dioxo-7lambda~4~-thiaspiro[4.4]non-7-ylidene)-5-methylisoxazole-4-carboxamide	3.3563	1.7469	0.037211	1.4293
Linamarin	3.3653	1.7507	0.011556	1.9372
apronalide	3.5349	1.8217	0.0032245	2.4915
1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoethanolamine	3.7794	1.9182	0.026769	1.5724
2-Aminooctanedioic acid	4.3141	2.1091	0.029085	1.5363
NP-020082	4.4218	2.1446	0.0015004	2.8238
ascr#29	4.887	2.289	0.0023789	2.6236
Xylenesulfonate	5.1788	2.3726	0.0073677	2.1327
1-myristoyl-2-palmitoleoyl-sn-glycero-3-phosphocholine	5.2837	2.4016	0.0036859	2.4335
5,6_-DIHYDRO PGI2	5.3633	2.4231	0.00045781	3.3393
6-{{2-(2-oxo-1-imidazolidinyl)ethyl}amino}-2-pyridinecarbonitrile	5.7456	2.5225	0.011824	1.9272
[Similar to: Victoria Pure Blue BO; _Mass: -222.1271 Da]	6.148	2.6201	0.0012249	2.9119
(4Z,16E,29E,31R)-15,31-Dihydroxy-4,16,29-tritriacontatriene-2,32-diyonic acid	6.2361	2.6406	0.0021701	2.6635
sphinganine-1-phosphocholine	6.2859	2.6521	0.00069728	3.1566
Taurochenodeoxycholic acid	7.0436	2.8163	0.021184	1.674
(S)-N-Boc-L-homoserine ethyl ester	9.6626	3.2724	0.00017725	3.7514
7-Methyl-6-thioguanosine	12.116	3.5989	0.0014088	2.8511

**Table S1.** Untargeted metabolomics analysis in colon tissue of mice exposed to polystyrene (2mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S1.

**Table S2.**

<b>Untargeted Metabolomic Analysis in Colon Tissue of Mice Exposed to Polystyrene (4mg/week) p = 0.05</b>	<b>FC</b>	<b>log2(FC)</b>	<b>raw.pval</b>	<b>-LOG10(p)</b>
<b>Lower</b>				
hexahydro-2-oxo-1h-thieno(3,4-d)imidazole-4-pentanoic acid	0.049435	-4.3383	0.00042841	3.3681
Homocarnosine	0.056165	-4.1542	0.0052136	2.2829
4-Hydroxy-4-(methylnitrosoamino)-1-(3-pyridinyl)-1-butanone	0.084394	-3.5667	0.0026376	2.5788
2-[(7-methyl-2,3-dihydro-1H-inden-4-yl)oxy]pyridin-3-amine	0.084394	-3.5667	0.0026376	2.5788
Zalcitabine	0.092094	-3.4408	0.0045502	2.342
2-Mercapto-3-methylbutan-1-ol	0.10784	-3.213	0.009004	2.0456
Carnosine	0.12284	-3.0252	0.0016398	2.7852
n-Hexanamide	0.12298	-3.0235	0.0111	1.9547
EIPA	0.14092	-2.827	0.0085784	2.0666
N-[(1S,3aS,5S,7aR)-7a-{3-[(2-Furylmethyl)amino]-3-oxopropyl}-5-hydroxy-3,3,5-trimethyloctahydro-1H-inden-1-yl]benzamide	0.1762	-2.5047	0.018036	1.7438
[Similar to: 4-Dodecylbenzenesulfonic acid; _Mass: -0.0364 Da]	0.2017	-2.3097	0.038908	1.41
Perindopril	0.2148	-2.2189	0.044594	1.3507
Clavam-2-carboxylate	0.23916	-2.0639	0.04329	1.3636
3-Hydroxysebacic acid	0.25386	-1.9779	0.019882	1.7015
2-Methyl-3-phenylpropyl hydrogen sulfate	0.29621	-1.7553	0.029485	1.5304
THTA	0.31297	-1.6759	0.039298	1.4056
1-(sn-glycero-3-phospho)-1D-myo-inositol	0.33887	-1.5612	0.0092024	2.0361
(1S,6S)-6-Aminoctahydro-1-indoliziny acetate	0.34988	-1.5151	0.046031	1.3369
bilirubin	0.39365	-1.345	0.028964	1.5381
9-Hexadecenoylcarnitine	0.40177	-1.3156	0.03599	1.4438
DA6495000	0.43482	-1.2015	0.04883	1.3113
1-Oleoyl-rac-glycerol	0.45994	-1.1205	0.03186	1.4968
Secnidazole	0.47635	-1.0699	0.032104	1.4934
<b>Higher</b>				
3-[(5Z)-5-Dodecenoyloxy]dodecanoic acid	2.0057	1.0041	0.041034	1.3869
3-(2,6-Dioxocyclohexyl)propanenitrile	2.0715	1.0507	0.03503	1.4556
N-Acetyl-L-phenylalanine	2.1389	1.0968	0.049383	1.3064
Mersalyl	2.1455	1.1013	0.018103	1.7422

[Similar to: L-Glutathione oxidized; _Mass: -225.0480 Da]	2.1716	1.1187	0.023221	1.6341
Amplex red	2.2387	1.1627	0.020239	1.6938
NSC 693868	2.2571	1.1745	0.038119	1.4189
Orotic acid	2.2632	1.1783	0.036991	1.4319
N-(Carboxymethyl)norleucine	2.2767	1.187	0.013437	1.8717
Crotanecine	2.3224	1.2156	0.0062499	2.2041
paeonilactone A	2.4339	1.2833	0.0075062	2.1246
Bromfenac	2.4694	1.3042	0.02167	1.6641
Primobolan	2.5069	1.3259	0.011789	1.9285
L-(+)-Aspartic acid	2.5222	1.3347	0.041542	1.3815
8-amino-2,6-anhydro-3,8-dideoxy-D-glycero-D-talo-octonic acid	2.5301	1.3392	0.023749	1.6244
Haplopine	2.5841	1.3696	0.01561	1.8066
N-Nitrosodiethylamine	2.64	1.4005	0.049468	1.3057
(2E)-N-[(3S)-2-Oxotetrahydro-3-furanyl]-2-dodecenamide	2.7089	1.4377	0.024827	1.6051
NSC 1775	2.7112	1.4389	0.033715	1.4722
Ethyl-_-D-glucuronide	2.7143	1.4406	0.019145	1.718
MFCD00210904	2.7262	1.4469	0.032908	1.4827
temurtide	2.7954	1.4831	0.022015	1.6573
O-Acetyl-L-serine	2.8016	1.4862	0.0069346	2.159
Pilocarpine	2.8142	1.4927	0.01615	1.7918
L-Glutamyl-L-Isoleucine	2.8278	1.4997	0.033939	1.4693
3-O-Methyl-N-acetyl-D-glucosamine	2.9215	1.5467	0.016568	1.7807
N-acetyldopamine	2.9607	1.5659	0.0026717	2.5732
Methyl (2R,3S)-3-hydroxy-8-methyl-8-azabicyclo[3.2.1]octane-2-carboxylate	3.0364	1.6024	0.045296	1.3439
4-amino-2-hydroxyamino-6-nitrotoluene	3.1258	1.6442	0.01252	1.9024
[Similar to: 2-benzylideneindan-1-one; _Mass: -7.9452 Da]	3.1531	1.6567	0.048809	1.3115
(5S,9R)-12-[(2R)-6-Hydroxy-2,5,7,8-tetramethyl-3,4-dihydro-2H-chromen-2-yl]-5,9-dimethyldodecanoic acid	3.1804	1.6692	0.0086491	2.063
CAY10665	3.1935	1.6751	0.026167	1.5822
DiQ	3.2208	1.6874	0.028777	1.541
2-[[[(3alpha,5beta,7alpha,8xi,12alpha)-3,7,12-Trihydroxy-24-oxocholan-24-yl]amino]ethyl hydrogen sulfate	3.3671	1.7515	0.0030144	2.5208
5-hydroxy-2,2,6,6-tetramethyl-4-{2-methyl-1-[2,4,6-trihydroxy-3-(2-methylpropanoyl)phenyl]propyl}cyclohex-4-ene-1,3-dione	3.5746	1.8378	0.045454	1.3424
trachelanthamidine	3.6633	1.8732	0.04212	1.3755
[Similar to: Taurodeoxycholic Acid (sodium salt); _Mass: -143.1652 Da]	3.6929	1.8848	0.046931	1.3285



_Estradiol-17_glucuronide	3.8107	1.9301	0.0022023	2.6571
1-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-8-methyl-1,2,3,4-tetrahydroquinoline	3.8631	1.9498	0.011186	1.9513
2-Aminooctanedioic acid	3.8863	1.9584	0.0090249	2.0446
N-5-Carboxypentyl-1-deoxynojirimycin	3.8899	1.9597	0.031626	1.5
NP-020082	4.3924	2.135	0.0066857	2.1749
beta-D-Ethyl glucuronide	4.8058	2.2648	0.014142	1.8495
Kojic acid	5.2644	2.3963	0.017637	1.7536
apronalide	5.4245	2.4395	0.018961	1.7221
(S)-N-Boc-L-homoserine ethyl ester	7.5054	2.9079	0.04455	1.3511
Pro-Lys	11.209	3.4866	0.03164	1.4998
Methionine sulfone	14.131	3.8208	0.026265	1.5806
7-Methyl-6-thioguanosine	17.119	4.0976	0.01952	1.7095
N-Acetylorithine	18.792	4.232	0.025229	1.5981

**Table S2.** Untargeted metabolomic analysis in colon tissue of mice exposed to polystyrene (4mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S2.

**Table S3.**

<b>Untargeted Metabolomic Analysis in Colon Tissue of Mice Exposed to Mixed Polymer (2mg/week) p = 0.05</b>	<b>FC</b>	<b>log2(FC)</b>	<b>raw.pval</b>	<b>-LOG10(p)</b>
<b>Lower</b>				
S-Lactoylglutathione	0.1429	-2.8069	0.0024224	2.6157
3-(Sulfooxy)butanoic acid	0.20343	-2.2974	0.021779	1.662
[Similar to: 2-benzylideneindan-1-one; _Mass: 1.0375 Da]	0.22513	-2.1512	0.0056007	2.2518
5'-O- {Hydroxy[(hydroxy{[hydroxy(phosphonoxy)phosphoryl]oxy}phosphoryl)oxy]phosphoryl]inosine	0.22567	-2.1477	0.046502	1.3325
2212914	0.22657	-2.142	0.036318	1.4399
Oxalosuccinic acid	0.28708	-1.8005	0.015077	1.8217
HC red 3	0.29058	-1.783	0.021922	1.6591
(1E)-1,7-bis(4-hydroxyphenyl)hept-1-en-3-one	0.3168	-1.6584	0.04937	1.3065
6-Isopropylidene-4,4a-dimethyl-7-oxodecahydro-2-naphthalenyl (2E)-3-(methylsulfonyl)acrylate	0.32579	-1.618	0.019881	1.7016
(1E)-4-(2-Thienyl)-1-buten-3-yn-1-ol	0.34259	-1.5454	0.049858	1.3023
(3Z)-4-(4-Methyl-1-piperaziny)-3-(2-oxopropylidene)-1,3-dihydro-2H-1,5-benzodiazepin-2-one	0.34401	-1.5395	0.027304	1.5638
butachlor [ANSI, JMAF, WSSA]	0.36245	-1.4641	0.027591	1.5592
L-Alanyl-L-glutamine	0.3673	-1.445	0.0043174	2.3648
S-methylglutathione	0.36861	-1.4398	0.01591	1.7983
[Similar to: (-)-Spiculisporic acid; _Mass: -0.0178 Da]	0.37036	-1.433	0.027159	1.5661
NP-001346	0.37069	-1.4317	0.0028182	2.55
[Similar to: ethyl 5-[(2,3-dihydro-1-benzofuran-5-ylsulfonyl)amino]-2-piperidinobenzoate; _Mass: -246.1395 Da]	0.37665	-1.4087	0.030737	1.5123
(4S,8S)-1-{1-[2-Amino-1-hydroxy-3-(4-hydroxycyclohexyl)propoxy]-2-pyrrolidiny]-4-[(2S)-2-butanyl]-12-(dihydroxymethyl)-1-hydroxy-8-(hydroxymethyl)-14-methyl-2,6,10-trioxo-3,7,11-triazapentadecane-5,9-dione	0.38294	-1.3848	0.017555	1.7556

[Similar to: 4-Dodecylbenzenesulfonic acid; _Mass: -0.0364 Da]	0.39178	-1.3519	0.022669	1.6446
1-Methyl-3,4-dihydro-6,7-isoquinolinediol	0.39187	-1.3515	0.0017522	2.7564
Metirosine	0.39391	-1.344	0.0019402	2.7121
S-Adenosylhomocysteine	0.39416	-1.3431	0.01445	1.8401
L-(-)-Methionine	0.40108	-1.318	0.035537	1.4493
Piperonyl sulfoxide	0.40282	-1.3118	0.035105	1.4546
L-Ergothioneine	0.41036	-1.285	0.034252	1.4653
5-Aminoisotonitazene	0.41191	-1.2796	0.02871	1.542
Tauropine	0.4125	-1.2775	0.010177	1.9924
2,4-Diaminotoluene	0.41341	-1.2744	0.025037	1.6014
Hypotaurine	0.42282	-1.2419	0.039494	1.4035
Paraldehyde	0.42956	-1.2191	0.026548	1.576
2-Methylthiazolidine	0.445	-1.1681	0.041315	1.3839
3-Methylsulfolene	0.44668	-1.1627	0.041007	1.3871
Methyl alpha-aspartylphenylalaninate	0.45525	-1.1353	0.013023	1.8853
dacisteine	0.45634	-1.1318	0.017736	1.7512
Secnidazole	0.46077	-1.1179	0.017444	1.7584
Linoleyl carnitine	0.47302	-1.08	0.0016362	2.7862
Guanine	0.47969	-1.0598	0.021185	1.674
CYCLO(L-LEU-L-PRO)	0.48302	-1.0498	0.019845	1.7023
Gonan-3-yl hydrogen sulfate	0.48653	-1.0394	0.047946	1.3193
Pivagabine	0.49189	-1.0236	0.017515	1.7566
asp-gln	0.49382	-1.0179	0.01277	1.8938
Ostruthin	0.49512	-1.0142	0.037659	1.4241
<b>Higher</b>				
N-Sulfanyl-L-asparagine	2.0003	1.0002	0.035408	1.4509
Nigrifactin	2.0272	1.0195	0.010057	1.9975
methylguanidine	2.0449	1.032	0.0045048	2.3463
C8-HSL	2.0557	1.0396	0.017832	1.7488
SA1850000	2.059	1.0419	0.038616	1.4132
VQH	2.0627	1.0446	0.03323	1.4785
N8-Acetylspermidine	2.071	1.0503	0.025357	1.5959
toluidine	2.0721	1.0511	0.028607	1.5435
3-hydroxy-3-methyloxindole	2.0752	1.0532	0.013712	1.8629
8-Hydroxyquinoline	2.0765	1.0542	0.013871	1.8579
6-Thio-dG	2.0832	1.0588	0.0072956	2.1369
_Alanine	2.098	1.069	0.047795	1.3206
19(R)-hydroxy Prostaglandin F1?	2.1063	1.0747	0.019671	1.7062
4-(Hydroxymethyl)benzenesulfonic acid	2.1114	1.0782	0.033353	1.4769
Methanesulfonic acid	2.1277	1.0893	0.01341	1.8726
Crotonic acid	2.1288	1.09	0.031703	1.4989
(9Z,11E)-13-[(4Z,7Z,10Z,16Z,19Z)-4,7,10,13,16,19-Docosahexaenoyloxy]-9,11-octadecadienoic acid	2.1351	1.0943	0.049103	1.3089

Ferulic acid 4-sulfate	2.1358	1.0947	0.034046	1.4679
Tridemorph	2.198	1.1362	0.025728	1.5896
Gentioflavine	2.2382	1.1623	0.014198	1.8478
m-carboxyaniline	2.2623	1.1778	2.54E-05	4.5959
6-Oxohexanoic acid	2.2823	1.1905	0.034902	1.4572
2-Hexenoylcarnitine	2.2995	1.2013	0.045521	1.3418
2,4,5-trimethoxyamphetamine	2.3057	1.2052	0.032819	1.4839
(2E)-3-Methyl-4-(sulfooxy)-2-butenic acid	2.3259	1.2178	0.036834	1.4337
1-Isothiocyanato-7-(methylthio)heptane	2.3354	1.2237	0.032892	1.4829
Isobutyric acid	2.4441	1.2893	0.0044778	2.3489
3-Buten-1-amine	2.4741	1.3069	0.001662	2.7794
Ethyl sulfate	2.5166	1.3315	0.028943	1.5385
Imidazoleacetic acid	2.5239	1.3356	0.037908	1.4213
(2S,3R)-N-(1-Hydroxy-2-propanyl)-2-methyl-3-pentadecyl-2-oxiranecarboxamide	2.5244	1.336	0.033877	1.4701
ODA	2.5338	1.3413	0.0071442	2.146
Anthranil	2.554	1.3527	6.21E-05	4.2071
acetyltaurine	2.5557	1.3537	0.010096	1.9958
(S)-(+)-allantoin	2.585	1.3702	0.02084	1.6811
Glycerone sulfate	2.5884	1.3721	0.0045225	2.3446
D-(+)-Xylose	2.6144	1.3865	0.0087848	2.0563
5-Butyloxazole	2.6351	1.3979	0.028359	1.5473
3-Indoxyl sulphate	2.6489	1.4054	0.01339	1.8732
Isoleucyl-4-hydroxyproline	2.686	1.4255	0.022949	1.6392
Sulfosalicylic Acid	2.7033	1.4347	0.0093032	2.0314
1-(2-Isopropylidenehydrazino)phthalazine	2.7313	1.4496	0.008294	2.0812
Dihydrouridine	2.8044	1.4877	0.013377	1.8736
AL9450000	2.8046	1.4878	0.023263	1.6333
D-Glucono-delta-lactone	2.907	1.5395	0.003871	2.4122
1,5-Isoquinolinediol	2.9189	1.5454	0.0015942	2.7975
2-Hydroxyethylclavam	2.9277	1.5498	0.015151	1.8196
(E)-2-Butenyl-4-methyl-threonine	2.9331	1.5524	0.04363	1.3602
4-Guanidinobutyric acid	2.9707	1.5708	0.008271	2.0824
Glycine	2.9774	1.5741	0.0056801	2.2456
fagaramide	2.9879	1.5791	0.042154	1.3752
4-ethylphenylsulfonic acid	2.9993	1.5846	0.041696	1.3799
4-Ethyl-2-hydroxy-6-methoxyphenyl hydrogen sulfate	2.9993	1.5846	0.041696	1.3799
[Similar to: 2-[(1H-1,2,4-triazol-3-ylimino)methyl]phenol; _Mass: -94.0626 Da]	2.9993	1.5846	0.041696	1.3799
3-Hydroxy-N-[(3S)-2-oxotetrahydro-3-furanyl]octanamide	3.0091	1.5893	0.014615	1.8352

Vanillic acid 4-sulfate	3.0258	1.5973	0.013024	1.8853
5-Aminovaleric acid	3.0615	1.6142	0.0098773	2.0054
3-Ureidopropionic acid	3.0744	1.6203	0.040765	1.3897
1-Methylimidazoleacetic acid	3.0925	1.6288	0.019158	1.7177
Terephthalic acid	3.1128	1.6382	0.022626	1.6454
4-cyclopropyl-6-methoxy-1,3,5-triazin-2-amine	3.1322	1.6472	0.0063034	2.2004
Trigonelline	3.1459	1.6535	0.00287	2.5421
PD 161570	3.1526	1.6565	0.0043092	2.3656
Gly-Lys	3.2074	1.6814	0.036549	1.4371
5-Hydantoinpropionic acid	3.2105	1.6828	0.03934	1.4052
(5Z)-2-Amino-4,5-dihydroxy-5-(((1E)-2-(hydroxymethyl)-1,3-butadien-1-yl)imino)pentanoic acid (non-preferred name)	3.2471	1.6991	0.040655	1.3909
5-Formyl-2-furoic acid	3.3044	1.7244	0.02717	1.5659
Cetrimonium	3.346	1.7425	0.047746	1.3211
2-Chloro-N-((2S,3R,4E)-1,3-dihydroxy-4-octadecen-2-yl)acetamide	3.4744	1.7968	0.00040168	3.3961
XJ6642800	3.5055	1.8096	0.013131	1.8817
N-Boc-L-proline	3.5079	1.8106	0.017005	1.7694
2,4-Dihydroxybenzoic acid	3.512	1.8123	0.0082057	2.0859
Formylisoglutamine	3.5217	1.8163	0.010361	1.9846
G-Lactone	3.5272	1.8185	2.90E-05	4.5382
MMDPPO	3.5454	1.826	0.0061883	2.2084
5-Nitro-o-toluidine	3.5587	1.8314	0.012697	1.8963
4-Hydroxy-3-methoxyphenylglycol sulfate	3.5942	1.8457	0.036239	1.4408
N-Acetylcitrulline	3.6691	1.8754	0.013102	1.8827
4-Phenolsulfonic acid	3.6912	1.8841	0.015513	1.8093
N5-(1-Iminoethyl)-L-ornithine	3.6966	1.8862	0.047833	1.3203
g-Guanidinobutyrate	3.6982	1.8868	0.0047823	2.3204
3-(Sulfooxy)benzenepropanoic acid	3.7081	1.8907	0.027015	1.5684
4-Acetamidobenzoic acid	3.7306	1.8994	0.02385	1.6225
Acetanilide	3.7471	1.9058	0.0066814	2.1751
2-oxo-8-methylthiooctanoic acid	3.7616	1.9114	0.0033344	2.477
Indole-3-carboxylic acid-O-sulphate	3.763	1.9119	0.01336	1.8742
N-Acetylornithine	3.8043	1.9276	0.041164	1.3855
3-hydroxy-2-methylbutyric acid	3.8638	1.95	0.015985	1.7963
[Similar to: N-(((1S,3R,4R,5S)-1,3,4-trihydroxy-5-(((phenylsulfonyl)acetyl)amino)cyclohexyl)carbonyl)-D-phenylalaninamide; _Mass: -354.1024 Da]	3.8653	1.9506	0.038353	1.4162
Benzenol	3.8706	1.9526	0.037393	1.4272
4-ACETAMIDOBUTYRIC ACID	3.91	1.9672	0.0055212	2.258

3,4-Dihydroxybenzenesulfonic acid	4.0908	2.0324	0.0041192	2.3852
ecgonone methyl ester	4.0924	2.0329	0.027835	1.5554
4-hydroxy Alternariol	4.1218	2.0433	0.0058224	2.2349
3-[4-(Sulfooxy)phenyl]acrylic acid	4.1746	2.0616	0.0059179	2.2278
Aceglutamide	4.2395	2.0839	0.0018623	2.7299
Methylhippuric acid	4.2818	2.0982	0.0011355	2.9448
Benalfocin	4.306	2.1063	0.0087295	2.059
Resorcinol	4.3205	2.1112	0.0078657	2.1043
4-Hydroxy-3-(sulfooxy)benzoic acid	4.4117	2.1413	0.0097759	2.0098
Hippuric acid	4.5592	2.1888	0.011043	1.9569
CAY10662	4.5924	2.1992	0.0027891	2.5545
doxapram	4.5986	2.2012	0.0027895	2.5545
4-(2-Hydroxyethyl)phenyl hydrogen sulfate	4.6036	2.2027	0.017526	1.7563
n-Hexanamide	4.6303	2.2111	0.034965	1.4564
Benzoic acid	4.635	2.2126	0.010647	1.9728
Zalcitabine	4.6667	2.2224	0.0066634	2.1763
alpha-Methyl D-mannoside	4.6672	2.2225	0.0086589	2.0625
5-sulfooxymethylfurfural	4.6742	2.2247	0.0031477	2.502
Arachidonoyl serotonin	4.734	2.2431	0.012233	1.9125
Oleana-12,21-dien-3-ol	4.7366	2.2439	0.012384	1.9071
APR-246	4.7518	2.2485	0.014671	1.8335
PRIMA-1	4.8081	2.2655	0.0043908	2.3575
1228222	4.8357	2.2737	0.0036848	2.4336
propionylcarnitine	4.8444	2.2763	0.013187	1.8798
MST-312	4.9233	2.2996	0.010235	1.9899
4-Acetamidobutanoic acid	4.9282	2.3011	0.00066374	3.178
(1'R,2'S,3S,5'S,6'S,8'R,11'S)-4'-Methyl-2'-vinylspiro[indole-3,7'-[9]oxa[4]azatetracyclo[6.3.1.0~2,6~.0~5,11~]dodecan]-2(1H)-one	5.0991	2.3502	0.0034563	2.4614
N-Acetyl-Trp-OH	5.1417	2.3623	0.0049573	2.3048
Benzyl 2-oxohexahydrocyclopropa[d]imidazole-1-carboxylate	5.1557	2.3662	0.0030753	2.5121
N-(3-acetamidopropyl)pyrrolidin-2-one	5.2809	2.4008	0.036782	1.4344
guaiacol sulfate	5.443	2.4444	0.00047187	3.3262
LUF6283	5.4734	2.4524	0.014105	1.8506
MFCD12912432	5.5905	2.483	0.0044572	2.3509
Kynurenic acid	5.6549	2.4995	0.0090399	2.0438
2,2'-Iminodipropan-1-ol	5.673	2.5041	0.017493	1.7571
(Z)-N-(1-Hydroxy-2-((Z)-[(2E)-1-hydroxy-3-(4-hydroxy-3-methoxyphenyl)-2-propen-1-ylidene]amino)ethylidene)phenylalanine	5.7005	2.5111	0.031468	1.5021
[4-(Sulfooxy)phenyl]acetic acid	5.7295	2.5184	0.0071609	2.145

[Similar to: 2-(4,4-diphenyl-1-piperidinobuta-1,3-dienyl)phenyl acetate; _Mass: -147.2111 Da]	5.7681	2.5281	0.031426	1.5027
3-[4-(Sulfooxy)phenyl]-2-oxiranecarboxylic acid	5.8032	2.5369	0.016739	1.7763
8-Amino-7-oxononanoic acid	5.8375	2.5454	0.00062902	3.2013
3-[3-Methoxy-4-(sulfooxy)phenyl]propanoic acid	5.8795	2.5557	0.0071155	2.1478
1774244	5.9159	2.5646	0.0013535	2.8685
2-Hydroxy-5-vinylphenyl hydrogen sulfate	5.9322	2.5686	0.015544	1.8084
GSK2879552	5.9451	2.5717	0.0015697	2.8042
4-Formyl-2-methoxyphenyl hydrogen sulfate	5.9994	2.5848	0.0034216	2.4658
3-Methoxy-4-hydroxyphenylethyleneglycol sulfate	6.0615	2.5997	0.01102	1.9578
Phenylacetyl glycine	6.0763	2.6032	0.0016056	2.7944
Lanthionine ketimine	6.1495	2.6205	0.003696	2.4323
N-Acetylvaline	6.2864	2.6522	0.00056461	3.2482
Butyryl-L-homoserine lactone	6.3339	2.6631	0.0028352	2.5474
Misonidazole	6.4012	2.6784	0.020713	1.6838
(+)-homotyrosine	6.4171	2.6819	0.0042415	2.3725
6-Methoxy-1H-indol-5-yl-D-glucopyranosiduronic acid	6.4643	2.6925	0.024686	1.6075
Dynone	6.474	2.6947	0.027811	1.5558
N-Acetyl-L-histidine	6.6125	2.7252	0.0065123	2.1863
(5E,7E)-8-Nitro-5,7-tetradecadienoic acid	6.6718	2.7381	0.0024718	2.607
Diethyl phenyl phosphate	6.7364	2.752	0.0073387	2.1344
hexobarbital	6.9577	2.7986	0.0045822	2.3389
Nicotinuric acid	6.9608	2.7993	0.003177	2.498
(5-Oxo-2-sulfo-2,5-dihydro-2-furanyl)acetic acid	7.0094	2.8093	0.007401	2.1307
Cinnamoyl glycine	7.1348	2.8349	0.0065327	2.1849
[Similar to: Alfentanil; _Mass: -252.1581 Da]	7.1705	2.8421	0.025474	1.5939
6,7,8-Trimethoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline	7.3413	2.876	0.00058043	3.2362
1-Methylpseudouridine	7.4523	2.8977	0.0058078	2.236
2-methoxyacetaminophen sulfate	7.5801	2.9222	0.0063136	2.1997
(2S)-3-Hydroxy-2-(((3S,4S,5R)-2,3,4-trihydroxy-5-(hydroxymethyl)tetrahydro-2-furanyl)methyl)amino)butanoic acid (non-preferred name)	7.7467	2.9536	0.029199	1.5346
8-Hydroxy-2-quinolinyl beta-D-glucopyranosiduronic acid	7.9942	2.9989	0.0037903	2.4213
3-(3,5-Dihydroxyphenyl)propanoyl hydrogen sulfate	8.0733	3.0132	0.0022612	2.6457



2,3-Dihydroxy-2-(4-hydroxy-3-methoxybenzyl)succinic acid	8.4205	3.0739	0.0027941	2.5538
Geranylarnesyl pyrophosphate	8.4433	3.0778	0.026998	1.5687
(6R,7S)-6,7-Dihydroxy-8-methyl-8-azabicyclo[3.2.1]oct-3-yl (2E)-2-methyl-2-butenolate	8.4566	3.0801	0.0012371	2.9076
gamma-thiomethyl glutamate	8.564	3.0983	0.0022531	2.6472
4-Aminopyridine	8.6267	3.1088	0.0022012	2.6573
3-Mercaptolactic acid	8.9398	3.1602	0.0032021	2.4946
Nitrosoheptamethyleneimine	9.955	3.3154	0.012131	1.9161
Aminohippuric acid	10.019	3.3247	0.001924	2.7158
S-OXY CYSTEINE	10.031	3.3265	0.019971	1.6996
N-Isovalerylglycine	10.116	3.3385	0.00090588	3.0429
Guanidinosuccinic acid	10.816	3.4351	0.038097	1.4191
5-ureidoimidazole-4-carboxylic acid	11.133	3.4768	0.0090902	2.0414
[Similar to: 5-(((1S,4S)-4-{3,5-Dimethyl-1-[4-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl}-2-cyclopenten-1-yl)amino)-3,3-dimethyl-5-oxopentanoic acid; _Mass: - 275.1538 Da]	11.223	3.4884	0.0098836	2.0051
acetylserine	11.268	3.4942	0.015744	1.8029
hexahydro-2-oxo-1h-thieno(3,4-d)imidazole-4-pentanoic acid	11.53	3.5273	0.0095516	2.0199
methyl-2-pyrimidinepropanoic acid	12.02	3.5873	0.0084813	2.0715
N-(5-Hydroxypentanoyl)glycine	12.297	3.6203	0.00089381	3.0488
L-Cysteic acid	12.502	3.644	0.017835	1.7487
2-Amino-4-[(3-aminopropyl)amino]butanoic acid	13.639	3.7697	0.013296	1.8763
Hexylbenzene	14.415	3.8495	0.00060135	3.2209
bendiocarb	15.744	3.9767	0.011314	1.9464
clavulanic acid	16.087	4.0078	0.028955	1.5383
L-Lysine lactam	16.365	4.0326	0.016746	1.7761
Methylenediurea	16.387	4.0345	0.0045529	2.3417
formylmethionine	16.409	4.0364	0.049884	1.302
p-Cresylsulfate	17.236	4.1073	6.80E-05	4.1673
[Similar to: (1'S,2'S)-3',11'-dihydroxy-1',2',5'-trimethyl-8'-oxaspiro[oxirane-2,12'-tricyclododecan]-5'-en-4'-one; _Mass: -0.1059 Da]	17.262	4.1095	0.0012334	2.9089
Caffeic acid 3-sulfate	17.979	4.1682	0.00064288	3.1919
Helicid	20.742	4.3745	2.61E-05	4.584
pyroglutamylglycine	20.998	4.3922	9.57E-05	4.0191
nitrilotriacetic acid	21.234	4.4083	0.0047563	2.3227
Methionine sulfone	21.713	4.4405	0.021251	1.6726
2-Aminooctanedioic acid	28.423	4.829	0.030362	1.5177

(2S,4S)-4-Amino-2-hydroxy-2-methylpentanedioic acid	49.859	5.6398	0.032039	1.4943
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**Table S3.** Untargeted metabolomic analysis in colon tissue of mice exposed to mixed polymer (2mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S3.

**Table S4.**

Untargeted Metabolomic Analysis in Colon Tissue of Mice Exposed to Mixed Polymer (4mg/week) p = 0.05	FC	log2(F C)	raw.pval	- LOG10(p)
<b>Lower</b>				
3-(Sulfooxy)butanoic acid	0.095148	-3.3937	0.0017433	2.7586
dilauroyl peroxide	0.10621	-3.235	0.0096062	2.0174
(5beta)-Chola-7,9(11)-dien-24-oic acid	0.12527	-2.9968	0.011634	1.9343
1-(16,17-Dimethoxyaspidospermidin-1-yl)ethanone	0.13459	-2.8934	0.014705	1.8325
3-{1-Hydroxy-2-[13-hydroxy-13-(hydroxymethyl)-8-methylpodocarpan-14-yl]ethyl}-5-oxo-2,5-dihydro-2-furanyl (2E)-3-phenylacrylate	0.13503	-2.8887	0.009863	2.006
BIBP-3226	0.16507	-2.5988	0.034498	1.4622
carzenide	0.16777	-2.5755	0.0093915	2.0273
Niacin	0.16806	-2.573	0.0017038	2.7686
BRACO-19	0.16944	-2.5611	0.010207	1.9911
delcorine	0.19735	-2.3411	0.0048058	2.3182
(1'R,2S,4'S,5S,6R,8'R,10'E,12'S,13'S,14'E,16'E,20'R,21'R,24'S)-6-[(2S)-2-Butanyl]-24'-hydroxy-21'-methoxy-5,11',13',22'-tetramethyl-2'-oxo-5,6-dihydrospiro[pyran-2,6'-[3,7,19]trioxatetracyclo[15.6.1.1~4,8~.0~20,24~]pentacosa[10,14,16,22]tetraen]-12'-yl 2,6-dideoxy-3-O-methyl-alpha-L-arabino-hexopyranoside	0.19758	-2.3395	0.0041709	2.3798
[Similar to: 4-Dodecylbenzenesulfonic acid; _Mass: - 0.0364 Da]	0.22078	-2.1793	0.00033977	3.4688
[Similar to: ethyl 5-[(2,3-dihydro-1-benzofuran-5-ylsulfonyl)amino]-2-piperidinobenzoate; _Mass: - 246.1395 Da]	0.22596	-2.1458	0.00097539	3.0108
Olean-18-en-3-yl (2E)-3-phenylacrylate	0.23625	-2.0816	0.0015303	2.8152
BRD6688	0.23666	-2.0791	0.000511	3.2916
stylisterol A	0.23685	-2.078	0.02616	1.5824
Rocuronium	0.24077	-2.0543	0.029075	1.5365
Leaf salicylate	0.24339	-2.0386	0.0037546	2.4254
BIX02189	0.24365	-2.0371	0.0037676	2.4239
exalamide	0.24472	-2.0308	0.032903	1.4828
Mono(2-ethylhexyl) phthalate (MEHP)	0.24774	-2.0131	0.00070673	3.1507

3-[2-[(E)-[3-(2-carboxylethyl)-5-[(4-ethyl-3-methyl-5-oxo-pyrrolidin-2-yl)methyl]-4-methyl-pyrrol-2-ylidene]methyl]-5-[(3-ethyl-4-methyl-5-oxo-pyrrolidin-2-yl)methyl]-4-methyl-1H-pyrrol-3-yl]propanoic acid	0.2518	-1.9896	0.0038898	2.4101
Adenine	0.25934	-1.9471	0.0068638	2.1634
N-undecanoyl-L-Homoserine lactone	0.26029	-1.9418	0.01499	1.8242
4-Amino-1-[(2xi)-5-O-{hydroxy[(hydroxy{(2R)-2-[(12-methyltetradecanoyl)oxy]-3-[(22-methyltricosanoyl)oxy]propoxy}phosphoryl)oxy]phosphoryl)-beta-D-threo-pentofuranosyl]-2(1H)-pyrimidinone	0.2659	-1.9111	0.018889	1.7238
14-(2,6-dihydroxy-6-methyl-3-oxoheptan-2-yl)-4,13-dihydroxy-1,6,6,11,15-pentamethyl-5-[[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy]tetracycloheptadec-7-en-17-one	0.28179	-1.8273	0.0053185	2.2742
(1E)-1,7-bis(4-hydroxyphenyl)hept-1-en-3-one	0.28308	-1.8207	0.018716	1.7278
6-Isopropylidene-4,4a-dimethyl-7-oxodecahydro-2-naphthalenyl (2E)-3-(methylsulfanyl)acrylate	0.28426	-1.8147	0.0088085	2.0551
butachlor [ANSI, JMAF, WSSA]	0.28442	-1.8139	0.0072924	2.1371
13,14-dihydro-15-keto-tetranor Prostaglandin D2	0.28833	-1.7942	0.0013354	2.8744
[Similar to: (-)-Spiculisporic acid; _Mass: -0.0178 Da]	0.28975	-1.7871	0.0068757	2.1627
(3Z)-4-(4-Methyl-1-piperazinyl)-3-(2-oxopropylidene)-1,3-dihydro-2H-1,5-benzodiazepin-2-one	0.29084	-1.7817	0.01077	1.9678
GINKGOLIDE C	0.304	-1.7178	0.0021156	2.6746
4-Undecylbenzenesulfonic acid	0.30433	-1.7163	0.018672	1.7288
2,4-Diaminotoluene	0.3135	-1.6734	0.01613	1.7924
(2S)-2-Hydroxy-3-(palmitoyloxy)propyl 6-deoxy-6-sulfo-alpha-D-glucopyranoside	0.31486	-1.6672	0.0055086	2.259
Levonorgestrel	0.31753	-1.6551	0.0082272	2.0847
Gonan-3-yl hydrogen sulfate	0.31978	-1.6448	0.003174	2.4984
(1E)-4-(2-Thienyl)-1-buten-3-yn-1-ol	0.31986	-1.6445	0.034786	1.4586
Piperonyl sulfoxide	0.33304	-1.5862	0.0061316	2.2124
Paraldehyde	0.33462	-1.5794	0.0065774	2.1819
6-[[6-Aminohexanoyl]amino]hexanoic acid	0.33509	-1.5774	0.018405	1.7351
Ostruthin	0.33676	-1.5702	0.0036879	2.4332
(4S,8S)-1-{1-[2-Amino-1-hydroxy-3-(4-hydroxycyclohexyl)propoxy]-2-pyrrolidinyl}-4-[(2S)-2-butanyl]-12-(dihydroxymethyl)-1-hydroxy-8-(hydroxymethyl)-14-methyl-2,6,10-trioxa-3,7,11-triazapentadecane-5,9-dione	0.34347	-1.5417	0.012001	1.9208
4-styrenesulfonic acid	0.34608	-1.5308	0.010342	1.9854
VU0071063	0.35076	-1.5115	0.024343	1.6136
IE1225000	0.35121	-1.5096	0.039263	1.406
6-Deoxypenciclovir	0.3523	-1.5051	0.025782	1.5887
Leu-Leu	0.35914	-1.4774	0.033331	1.4772
[Similar to: 2-benzylideneindan-1-one; _Mass: -9.9663 Da]	0.37956	-1.3976	0.013403	1.8728

[Similar to: Sphingosine (d18:1); _Mass: -0.1187 Da]	0.38151	-1.3902	0.016492	1.7827
4-Dodecylbenzenesulfonic acid	0.38577	-1.3742	0.0036379	2.4392
5?-androstane-3?,17?-diol dipropionate	0.38601	-1.3733	0.044932	1.3474
beta-L-fucose 1-phosphate	0.39333	-1.3462	0.0095434	2.0203
15-Deoxy-_12,14 -Prostaglandin J2	0.39352	-1.3455	0.044031	1.3562
PALGLY	0.40288	-1.3116	0.033661	1.4729
[Similar to: N1-{5-[(4-chlorophenyl)thio]-4-fluoro-2-nitrophenyl}acetamide; _Mass: 0.1981 Da]	0.41443	-1.2708	0.0009935 9	3.0028
Ro 18-5364	0.41712	-1.2614	0.01564	1.8058
Guanosine	0.42065	-1.2493	0.0044839	2.3483
FENOFIBRATE-D6	0.42658	-1.2291	0.0056736	2.2461
Glycyl-L-leucine	0.43006	-1.2174	0.0023628	2.6266
[Similar to: Guanosine; _Mass: 36.9799 Da]	0.44437	-1.1702	0.012108	1.9169
[Similar to: Guanosine; _Mass: 35.9766 Da]	0.4527	-1.1434	0.010069	1.997
Oxacycloheptacosan-2-one	0.45302	-1.1424	0.034008	1.4684
Guanine	0.45422	-1.1385	0.011446	1.9414
HP1760000	0.46769	-1.0964	0.045773	1.3394
Phenelzine	0.47869	-1.0628	0.033802	1.4711
alpha-D-Mannopyranosyl-(1->4)-6-deoxy-alpha-L-mannopyranosyl-(1->3)-1-O-{hydroxy[(hydroxy[(2Z,6Z,10Z,14Z,18Z,22Z,26Z,30Z,34E,38E)-3,7,11,15,19,23,27,31,35,39,43-undecamethyl-2,6,10,14,18,22,26,30,34,38,42-tetratetracontaundecaen-1-yl]oxy]phosphoryl)oxy]phosphoryl}-alpha-D-galactopyranose	0.48916	-1.0316	0.010245	1.9895
Pimodivir	0.49574	-1.0123	0.044885	1.3479
L-Alanyl-L-glutamine	0.4983	-1.0049	0.022287	1.652
Timonacic	0.49901	-1.0029	0.025717	1.5898
<b>Higher</b>				
Creatinine	2.0165	1.0119	0.0030364	2.5176
carglumic acid	2.0587	1.0417	0.036757	1.4347
tetramethyl Nordihydroguaiaretic Acid	2.1222	1.0855	0.0057664	2.2391
acetyltaurine	2.1496	1.1041	0.020445	1.6894
N3,N4-Dimethyl-L-arginine	2.1552	1.1078	0.0035976	2.444
9,10-Dihydroxy-11-(3-pentyl-2-oxiranyl)undecanoic acid	2.1592	1.1105	0.0064494	2.1905
L-alpha-lysophosphatidylcholine	2.1639	1.1136	0.040638	1.3911
2-Chloro-N-[(2S,3R,4E)-1,3-dihydroxy-4-octadecen-2-yl]acetamide	2.204	1.1401	0.031375	1.5034
4-Ethyl-2,6-dihydroxyphenyl hydrogen sulfate	2.2912	1.1961	0.0076246	2.1178
Aminoparathion	2.2956	1.1989	0.031467	1.5021
bendiocarb	2.312	1.2091	0.039767	1.4005
Nigrifactin	2.3154	1.2112	0.043521	1.3613
4-Amino-4-deoxypentopyranose	2.3246	1.217	0.0029461	2.5307
3-methylthymine	2.3471	1.2309	0.044578	1.3509

D-Xyloic acid	2.3608	1.2393	0.018445	1.7341
m-carboxyaniline	2.3616	1.2398	0.0093415	2.0296
N-Acetylhistamine	2.3846	1.2538	0.019667	1.7063
(2R)-2-Hydroxy-3-[(1Z)-1-tetradecen-1-yloxy]propyl 2-(trimethylammonio)ethyl phosphate	2.3978	1.2617	0.027499	1.5607
Dihydroartemisinin	2.4326	1.2825	0.01127	1.9481
Buprenorphine	2.4351	1.284	0.0050564	2.2962
Vanillin	2.4682	1.3034	0.047467	1.3236
2,2'-Iminodipropan-1-ol	2.4918	1.3172	0.036507	1.4376
Glycylproline	2.5011	1.3225	0.0007880 2	3.1035
Indole-3-acetic acid	2.5075	1.3262	0.034425	1.4631
M2I-1	2.5295	1.3389	0.021396	1.6697
Glycocyamine	2.567	1.3601	0.028239	1.5492
Imazapyr	2.584	1.3696	0.036621	1.4363
[Similar to: L-(-)-Malic acid; _Mass: 97.9674 Da]	2.5983	1.3776	0.006943	2.1585
N-(tert-Butyl)-N'-(2-hydroxyethyl)urea	2.6084	1.3831	0.043697	1.3596
N,N-Dihydroxy-L-valine	2.6106	1.3844	0.0029355	2.5323
6,7,8-Trimethoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline	2.625	1.3923	0.012103	1.9171
ENU	2.6526	1.4074	0.016508	1.7823
N-(4-Heptanyl)-1,3-benzodioxole-5-carboxamide	2.6576	1.4101	0.03401	1.4684
2,2'-Sulfinyldiacetic acid	2.6684	1.416	0.017801	1.7496
3-Butene-1,2,3-tricarboxylic acid	2.6969	1.4313	0.01825	1.7387
Itaconic acid	2.7164	1.4417	0.0030147	2.5208
(9Z,11E)-13-[(4Z,7Z,10Z,16Z,19Z)-4,7,10,13,16,19-Docosahexaenoxy]-9,11-octadecadienoic acid	2.7218	1.4445	0.0033589	2.4738
(-)-(alpha)-Kainic Acid	2.7389	1.4536	0.018663	1.729
L-Iditol	2.7436	1.4561	0.0062376	2.205
N-Isovalerylglycine	2.7841	1.4772	0.0046369	2.3338
metioprim	2.7937	1.4822	0.0034215	2.4658
4-Hydroxyprolylleucine	2.8045	1.4877	0.041946	1.3773
3-Sulfamoylalanine	2.8107	1.4909	0.0073505	2.1337
L-Cladinpyranose	2.8304	1.501	0.027472	1.5611
1-(1Z-hexadecenyl)-sn-glycero-3-phosphocholine	2.8465	1.5092	0.0013023	2.8853
MMDPPO	2.9129	1.5424	0.0091258	2.0397
Crotonic acid	2.9334	1.5526	0.0082679	2.0826
RH0365500	2.979	1.5748	0.012905	1.8892
Anthranil	2.9956	1.5828	0.0040302	2.3947
g-Guanidinobutyrate	3.0259	1.5974	0.0059721	2.2239
[Similar to: 2-benzylideneindan-1-one; _Mass: 42.0277 Da]	3.032	1.6002	0.038013	1.4201
3-Hydroxysebacic acid	3.0504	1.609	0.01516	1.8193
Aceglutamide	3.068	1.6173	0.007334	2.1347
D-(+)-Xylose	3.1494	1.6551	0.024709	1.6071
(Hydroxyethyl)methacrylate	3.1651	1.6622	0.035069	1.4551

N6,N6,N6-Trimethyl-L-lysine	3.1754	1.6669	0.023384	1.6311
Methyl (10E)-11-(6-ethyl-2,3-dioxabicyclo[2.2.1]hept-5-yl)-9-hydroperoxy-10-undecenoate	3.1797	1.6689	0.017603	1.7544
4-(Hydroxymethyl)benzenesulfonic acid	3.2178	1.6861	0.0018735	2.7273
3-Buten-1-amine	3.2757	1.7118	0.0038976	2.4092
2271703	3.2775	1.7126	0.032416	1.4892
(6R,7S)-6,7-Dihydroxy-8-methyl-8-azabicyclo[3.2.1]oct-3-yl (2E)-2-methyl-2-butenolate	3.2981	1.7216	0.0002438 1	3.6129
Glycerone sulfate	3.3053	1.7248	0.0066425	2.1777
N-Hydroxy-meIQX	3.3653	1.7507	0.0067172	2.1728
4-Aminopyridine	3.4576	1.7898	0.0039223	2.4065
PD 161570	3.4933	1.8046	0.044556	1.3511
3-Hydroxy-N-[(3S)-2-oxotetrahydro-3-furanyl]octanamide	3.4938	1.8048	0.0049527	2.3052
nitrilotriacetic acid	3.571	1.8363	0.0090249	2.0446
C8-HSL	3.5743	1.8377	0.043975	1.3568
D-( <u>  </u> )-Erythrose	3.6025	1.849	0.031701	1.4989
[Similar to: 2-(4,4-diphenyl-1-piperidinobuta-1,3-dienyl)phenyl acetate; _Mass: 185.1721 Da]	3.6665	1.8744	0.010598	1.9748
Crotanecine	3.683	1.8809	0.0024184	2.6165
635994	3.8493	1.9446	0.0017784	2.75
bisbenzimidazole	3.8582	1.9479	0.049136	1.3086
hexahydro-2-oxo-1h-thieno(3,4-d)imidazole-4-pentanoic acid	3.8605	1.9488	0.0001039	3.9834
Methylsuccinic acid	3.9223	1.9717	0.013101	1.8827
4-Acetamidobutanoic acid	3.9586	1.985	0.0023475	2.6294
4-Oxo-4-(3-pyridyl)butyric acid	3.9724	1.99	0.042446	1.3722
4-ACETAMIDO BUTYRIC ACID	3.9752	1.991	0.0051833	2.2854
VQH	3.9975	1.9991	0.014582	1.8362
SA1850000	4.016	2.0058	0.0029421	2.5313
methyl-2-pyrimidinepropanoic acid	4.0275	2.0099	7.88E-05	4.1036
[Similar to: Flavin adenine dinucleotide (FAD); _Mass: -589.2222 Da]	4.0414	2.0148	0.012379	1.9073
19(R)-hydroxy Prostaglandin F1?	4.042	2.0151	0.018437	1.7343
Formylisoglutamine	4.1949	2.0686	0.028277	1.5486
Gentioflavine	4.2289	2.0803	0.01177	1.9292
Oleandrose	4.2444	2.0856	0.032668	1.4859
4-Guanidinobutyric acid	4.2887	2.1005	0.0099257	2.0032
Terephthalic acid	4.4103	2.1409	0.0007951 4	3.0996
[Similar to: Alfentanil; _Mass: -252.1581 Da]	4.4161	2.1428	0.031031	1.5082
1-(2-Isopropylidenehydrazino)phthalazine	4.4359	2.1492	0.0001742 8	3.7588
Glycine	4.4737	2.1615	0.0008438 2	3.0738
Uridine 5'-diphosphoglucuronic acid	4.5325	2.1803	0.045521	1.3418

N-Acetylgalactosamine 6-sulfate	4.5358	2.1813	0.0093558	2.0289
BD-AcAc2	4.6237	2.209	0.0023948	2.6207
Isoleucyl-4-hydroxyproline	4.6699	2.2234	0.017109	1.7668
5-Formyl-2-furoic acid	4.7406	2.2451	0.0006345	3.1976
deaminoneuraminic acid	4.8331	2.273	0.023837	1.6228
DL-Cerulenin	4.9243	2.2999	0.037886	1.4215
4-hydroxy Alternariol	4.9282	2.3011	0.001071	2.9702
Ferulic acid 4-sulfate	5.0463	2.3352	0.006019	2.2205
5-Butyloxazole	5.048	2.3357	0.011452	1.9411
5-sulfooxymethylfurfural	5.0604	2.3392	0.0052092	2.2832
Trigonelline	5.0823	2.3455	0.014828	1.8289
3-Indoxyl sulphate	5.1008	2.3507	0.002502	2.6017
Sulfosalicylic Acid	5.1667	2.3692	0.0027885	2.5546
1-Methylimidazoleacetic acid	5.1667	2.3692	0.031447	1.5024
Acetanilide	5.1693	2.37	0.0012557	2.9011
tensyucic acid E	5.2238	2.3851	0.0041377	2.3832
N-Acetylvaline	5.2558	2.3939	0.0010582	2.9754
4-Acetamidobenzoic acid	5.2591	2.3948	0.010648	1.9727
(5Z)-2-Amino-4,5-dihydroxy-5-(((1E)-2-(hydroxymethyl)-1,3-butadien-1-yl]imino}pentanoic acid (non-preferred name)	5.3467	2.4187	0.0031293	2.5046
N-Acetyl-Trp-OH	5.4446	2.4448	0.003726	2.4288
Isobutyric acid	5.4457	2.4451	0.0038422	2.4154
(S)-(+)-allantoin	5.4926	2.4575	0.018391	1.7354
4-ethylphenylsulfonic acid	5.5269	2.4665	0.027205	1.5654
4-Ethyl-2-hydroxy-6-methoxyphenyl hydrogen sulfate	5.5269	2.4665	0.027205	1.5654
[Similar to: 2-[(1H-1,2,4-triazol-3-ylimino)methyl]phenol; _Mass: -94.0626 Da]	5.5269	2.4665	0.027205	1.5654
Ethyl sulfate	5.5681	2.4772	0.0009064 8	3.0426
LOC14	5.6068	2.4872	0.0068927	2.1616
Nicotinyl methylamide	5.7083	2.5131	0.017722	1.7515
5-Hydantoinpropionic acid	5.8782	2.5554	0.038521	1.4143
3-hydroxy-2-methylbutyric acid	5.8808	2.556	0.029738	1.5267
Vanillic acid 4-sulfate	5.9509	2.5731	0.0047401	2.3242
3,4-Dihydroxybenzenesulfonic acid	5.9711	2.578	0.0086531	2.0628
Pal-GHK	6.0086	2.587	0.0030019	2.5226
Allantoin	6.0375	2.5939	0.015391	1.8127
Methylhippuric acid	6.0384	2.5942	0.0005570 7	3.2541
(5E,7E)-8-Nitro-5,7-tetradecadienoic acid	6.1384	2.6179	0.0029804	2.5257
2,4,5-trimethoxyamphetamine	6.1579	2.6224	0.034681	1.4599
MST-312	6.2622	2.6467	0.0013664	2.8644
Resorcinol	6.4386	2.6868	0.011959	1.9223
3-Hydroxy-5-methyl-L-tyrosine	6.6964	2.7434	0.0279	1.5544
6-Acetamido-2-oxohexanoic acid	6.7501	2.7549	0.0049168	2.3083



N-Acetyl-L-histidine	6.7888	2.7632	0.017139	1.766
Saccharin	6.9465	2.7963	0.030045	1.5222
Hippuric acid	6.9564	2.7983	0.0075353	2.1229
3-(Sulfooxy)benzenepropanoic acid	6.9812	2.8035	0.0096742	2.0144
Dihydrouridine	7.0034	2.8081	0.0056296	2.2495
(Z)-N-(1-Hydroxy-2-((Z)-[(2E)-1-hydroxy-3-(4-hydroxy-3-methoxyphenyl)-2-propen-1-ylidene]amino)ethylidene)phenylalanine	7.1965	2.8473	0.0039821	2.3999
Butyryl-L-homoserine lactone	7.2691	2.8618	0.0026768	2.5724
Resorcinolnaphthalein	7.2875	2.8654	0.018378	1.7357
[Similar to: 3-Coumaric acid; _Mass: 79.9760 Da]	7.323	2.8724	0.026879	1.5706
N-Boc-L-proline	7.362	2.8801	0.0049434	2.306
Nitrosoheptamethyleneimine	7.4101	2.8895	0.0076818	2.1145
PRIMA-1	7.4287	2.8931	0.0099132	2.0038
3-[4-(Sulfooxy)phenyl]acrylic acid	7.4859	2.9042	0.0019974	2.6995
Xanthurenic acid	7.5441	2.9154	0.0005592 1	3.2524
Cinnamoyl glycine	7.6344	2.9325	0.0076964	2.1137
Hexylbenzene	7.646	2.9347	0.0004245 8	3.372
Benzoic acid	7.7254	2.9496	0.004684	2.3294
L-Ascorbic acid 2-sulfate	7.9089	2.9835	0.0095467	2.0201
3-Hydroxysuberic acid	7.9123	2.9841	0.04755	1.3228
_Alanine	8.1149	3.0206	0.043069	1.3658
4-Methylphenol	8.1265	3.0226	3.95E-05	4.4029
N-Acetylcitrulline	8.2993	3.053	0.012438	1.9053
Benzyl 2-oxohexahydrocyclopropa[d]imidazole-1-carboxylate	8.3022	3.0535	0.0025046	2.6013
Zalcitabine	8.467	3.0818	0.0027773	2.5564
4-Phenolsulfonic acid	8.5363	3.0936	0.002789	2.5546
3-hydroxy-3-(3-hydroxyphenyl)propanoic acid-O-sulphate	8.5502	3.096	0.036783	1.4343
MFCD12912432	8.615	3.1068	0.0026428	2.5779
8-Amino-7-oxononanoic acid	8.8147	3.1399	6.38E-06	5.1954
Benalfocin	9.0922	3.1846	0.0039254	2.4061
guaiacol sulfate	9.3351	3.2227	0.0007749 5	3.1107
Gly-Lys	9.603	3.2635	0.0045528	2.3417
6-Methoxy-1H-indol-5-yl-D-glucopyranosiduronic acid	9.6428	3.2694	0.006175	2.2094
[Similar to: 7-Oxobenz[de]anthracene; _Mass: 6.9939 Da]	9.6655	3.2728	0.039056	1.4083
4-Acetamido-2-amino-6-nitrotoluene	9.7175	3.2806	0.017133	1.7662
alpha-Methyl D-mannoside	9.9595	3.3161	0.0022403	2.6497
5-Nitro-o-toluidine	9.9738	3.3181	0.0006537 7	3.1846

Aminohippuric acid	10.144	3.3425	0.0009334 1	3.0299
N5-(1-Iminoethyl)-L-ornithine	10.212	3.3522	0.0007303 2	3.1365
(+)-homotyrosine	10.284	3.3623	0.0058653	2.2317
APR-246	10.314	3.3665	0.010134	1.9942
propionylcarnitine	10.515	3.3944	0.009279	2.0325
xanthurenic acid 8-O-sulfate	10.61	3.4074	0.041436	1.3826
1-Methylpseudouridine	10.616	3.4082	0.010099	1.9957
4-(2-Hydroxyethyl)phenyl hydrogen sulfate	10.961	3.4544	0.0023775	2.6239
Benzenol	11.127	3.476	0.0011497	2.9394
hexobarbital	11.192	3.4844	0.0047492	2.3234
Lanthionine ketimine	11.27	3.4945	0.0051772	2.2859
2616	11.426	3.5142	0.03526	1.4527
Phenylacetylglucine	11.559	3.531	0.0008564 8	3.0673
Homocitrulline	11.657	3.5432	0.024868	1.6044
Nicotinuric acid	12.253	3.6151	0.001743	2.7587
2-methoxyacetaminophen sulfate	12.557	3.6504	0.0032044	2.4943
3-[3-Methoxy-4-(sulfooxy)phenyl]propanoic acid	12.809	3.6791	0.0064729	2.1889
4-Hydroxy-3-(sulfooxy)benzoic acid	12.9	3.6893	0.0027526	2.5602
Kynurenic acid	13.026	3.7033	0.01588	1.7992
[Similar to: N_ -{[(1S,3R,4R,5S)-1,3,4-trihydroxy-5- {[(phenylsulfonyl)acetyl]amino}cyclohexyl]carbonyl}-D- phenylalaninamide; _Mass: -354.1024 Da]	13.242	3.727	0.041634	1.3805
3-[4-(Sulfooxy)phenyl]-2-oxiranecarboxylic acid	13.993	3.8066	0.0049956	2.3014
2,3-Dihydroxy-2-(4-hydroxy-3-methoxybenzyl)succinic acid	14.004	3.8077	0.001926	2.7153
2-Hydroxy-5-vinylphenyl hydrogen sulfate	14.128	3.8205	0.0039102	2.4078
Diethyl phenyl phosphate	14.131	3.8208	0.0051974	2.2842
1228222	14.282	3.8362	0.0070422	2.1523
4-Formyl-2-methoxyphenyl hydrogen sulfate	14.333	3.8413	0.0033821	2.4708
3-Ureidopropionic acid	14.762	3.8838	0.010498	1.9789
Ribazole 5-phosphate	15.646	3.9677	0.0023597	2.6271
[4-(Sulfooxy)phenyl]acetic acid	15.678	3.9707	0.0020764	2.6827
3-Methoxy-4-hydroxyphenylethyleneglycol sulfate	15.767	3.9789	0.0056204	2.2502
8-Hydroxy-2-quinolinyl beta-D-glucopyranosiduronic acid	15.994	3.9994	0.0029979	2.5232
3-(3,5-Dihydroxyphenyl)propanoyl hydrogen sulfate	17.442	4.1245	0.0034464	2.4626
3-Mercaptolactic acid	18.133	4.1805	0.0001172 5	3.9309
1774244	18.577	4.2154	0.0002081 9	3.6815
5-ureidoimidazole-4-carboxylic acid	19.573	4.2908	0.031797	1.4976
4-Hydroxy-3- methoxyphenylglycol sulfate	24.12	4.5921	0.016475	1.7832

[Similar to: (1'S,2'S)-3',11'-dihydroxy-1',2',5'-trimethyl-8'-oxaspiro[oxirane-2,12'-tricyclododecan]-5'-en-4'-one; _Mass: -0.1059 Da]	34.811	5.1215	0.0039876	2.3993
Helicid	38.867	5.2805	1.12E-06	5.9495
Caffeic acid 3-sulfate	39.916	5.3189	0.0057502	2.2403
(5-Oxo-2-sulfo-2,5-dihydro-2-furanyl)acetic acid	43.55	5.4446	0.012707	1.8959
p-Cresylsulfate	51.917	5.6981	3.19E-06	5.4968

**Table S4.** Untargeted metabolomic analysis in colon tissue of mice exposed to mixed polymer microspheres (4mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S4.

**Table S5.**

Untargeted Metabolomic Analysis in Liver Tissue of Mice Exposed to Polystyrene (2mg/week) p = 0.05	FC	log2(FC)	raw.pval	- LOG10(p)
<b>Lower</b>				
pro-trp	0.12397	-3.012	4.05E-06	5.3928
DL-2,6-Diaminopimelic acid	0.16808	-2.5728	0.0002662	3.5748
pro-met	0.18241	-2.4548	0.0017532	2.7562
PGB1	0.19182	-2.3822	2.20E-05	4.6577
Ectoine	0.22612	-2.1448	0.00011439	3.9416
Glycylnorvaline	0.22612	-2.1448	0.00011439	3.9416
3-Thiomorpholinecarboxylic acid	0.22969	-2.1222	8.18E-06	5.0875
[Similar to: 5,7-dihydroxy-3-(4-hydroxyphenyl)-6-methoxy-4H-chromen-4-one; _Mass: -24.9442 Da]	0.22975	-2.1219	0.02324	1.6338
ALA-GLU	0.23002	-2.1202	0.00018982	3.7217
N-acetyl-beta-D-glucosaminyamine	0.23913	-2.0642	1.11E-05	4.9537
5,6-Dihydroxy-3-methyl-2(1H)-quinolinone	0.24505	-2.0289	0.00036541	3.4372
thr-arg	0.24695	-2.0177	9.26E-05	4.0333
ser-arg	0.25696	-1.9604	0.0001399	3.8542
Kynurenine	0.26096	-1.9381	0.00032779	3.4844
N-(2-Methoxyethyl)-3-{5-[(2S)-1-methyl-2-pyrrolidinyl]-1,2,4-oxadiazol-3-yl}-2-pyridinamine	0.26365	-1.9233	0.00031134	3.5068
Aceglutamide	0.27699	-1.8521	0.0068355	2.1652
2-[2-oxo-2-(pyridin-3-ylamino)ethoxy]acetic acid	0.28021	-1.8354	0.0038585	2.4136
Gly-Arg	0.2856	-1.8079	0.00037314	3.4281
Physovenine	0.28729	-1.7994	0.0025123	2.5999
beta-Alanyl-L-arginine	0.289	-1.7908	6.34E-05	4.1977
MFCD00025555	0.29144	-1.7788	2.17E-05	4.6627
Threonylglutamine	0.29448	-1.7638	0.00010108	3.9953
(15Z,19R)-25-Amino-22-hydroxy-22-oxido-17,21,23-trioxa-22lambda~5~-phosphapentacos-15-en-19-yl (9Z)-9-pentadecenoate	0.29758	-1.7487	7.06E-05	4.1513
b-Ala-Lys	0.29919	-1.7409	0.00030653	3.5135
(2S,3R,5S)-3-(2-Aminoethyl)-7-oxo-4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylic acid	0.30098	-1.7323	0.00010915	3.962
ser-asn	0.30568	-1.7099	8.38E-05	4.077
Protoporphyrin IX	0.30764	-1.7007	0.0016924	2.7715
ethyl 2-cyano-3-(3-pyridinyl)acrylate	0.31518	-1.6657	0.0017776	2.7502
afegostat	0.31721	-1.6565	8.50E-06	5.0705
Glycyl-L-leucine	0.31721	-1.6565	8.50E-06	5.0705
(2R,6S)-2,6-Diamino-3-hydroxyheptanedioic acid	0.31742	-1.6555	3.76E-05	4.4248

Tetrahydrouridine	0.31941	-1.6465	0.0022519	2.6474
4,10-Undecadiynal	0.32785	-1.6089	0.0014915	2.8264
Methylphenidate	0.33208	-1.5904	0.00014496	3.8387
meprobamate	0.33289	-1.5869	0.00032404	3.4894
S-Aminoethyl-L-cysteine	0.33747	-1.5672	0.027284	1.5641
ser-gln	0.33968	-1.5577	2.62E-05	4.5816
Phenylalanylglycine	0.35301	-1.5022	0.00027616	3.5588
Gly-Phe	0.35318	-1.5015	0.0013385	2.8734
UAMC-3203	0.36191	-1.4663	0.00066457	3.1775
Gibberellin A12 aldehyde	0.36959	-1.436	0.00035791	3.4462
Lacinilene C 7-methyl ether	0.37256	-1.4244	0.0033334	2.4771
P505-15	0.37541	-1.4135	0.0090694	2.0424
ALA-PRO	0.37792	-1.4038	0.00058306	3.2343
Glycine	0.37859	-1.4013	0.0046223	2.3351
N-Acetyl-D-alloisoleucine	0.38033	-1.3947	0.0022216	2.6533
methocarbamol	0.38241	-1.3868	0.008678	2.0616
Dodecanedioic acid	0.38657	-1.3712	0.02033	1.6919
Desthiobiotin	0.39559	-1.3379	0.00027421	3.5619
EDDA	0.40463	-1.3053	6.31E-05	4.2001
4-guanidinobutanal	0.40551	-1.3022	0.017318	1.7615
Acetylcarnitine	0.40621	-1.2997	0.00018805	3.7257
Glycerol 3-phosphate	0.40801	-1.2933	0.021303	1.6716
Rimantadine	0.40813	-1.2929	5.13E-05	4.2901
N-Acetyl-L-glutamine	0.40822	-1.2926	0.013505	1.8695
Lanost-8-ene-2,3,12,21,24,25-hexol	0.40848	-1.2917	0.0052515	2.2797
2-[(9Z)-9-Nonadecenoylamino]ethanesulfonic acid	0.41134	-1.2816	0.0032107	2.4934
pro-his	0.41388	-1.2727	0.00099008	3.0043
(+/-)-9-HpODE	0.41573	-1.2663	0.0016992	2.7698
N-Undecanoylglycine	0.41881	-1.2556	0.040219	1.3956
Ser-Ser	0.41884	-1.2555	0.00028616	3.5434
Val-Leu	0.42057	-1.2496	0.00042156	3.3751
YYA-021	0.4274	-1.2263	0.0075828	2.1202
Ethyl docosaehaenoate	0.43076	-1.215	0.0015293	2.8155
Leucylproline	0.43408	-1.204	9.99E-05	4.0003
Ser-Glu	0.43679	-1.195	1.28E-05	4.8933
(+)-castanospermine	0.44172	-1.1788	0.0022448	2.6488
Valylproline	0.44802	-1.1584	0.0014898	2.8269
Phenylisocyanate	0.45085	-1.1493	0.016183	1.7909
deaminoneuraminic acid	0.45182	-1.1462	0.0080747	2.0929
Valylvaline	0.453	-1.1424	0.0018513	2.7325
Gly-l-pro	0.45921	-1.1228	0.001736	2.7604
AMPA	0.46505	-1.1045	0.030987	1.5088
Glycylglutamine	0.46505	-1.1045	0.030987	1.5088
gamma-Glu-gln	0.46872	-1.0932	0.0060277	2.2198
HEPES	0.47335	-1.079	0.0015211	2.8179
Pro-Lys	0.47952	-1.0603	0.00047904	3.3196

PKF118-310	0.48	-1.0589	0.021656	1.6644
DL-Glutamine	0.48034	-1.0579	0.00029182	3.5349
4-Aminobenzoic acid	0.48063	-1.057	0.014296	1.8448
Methionylleucine	0.48359	-1.0481	0.02574	1.5894
Eldecalcitol	0.48788	-1.0354	0.037663	1.4241
EPK	0.48924	-1.0314	2.69E-05	4.5705
Gly-Lys	0.48931	-1.0312	0.01556	1.808
2-(3,4-Dihydroxyphenyl)-8-(beta-D-threo-hexopyranosyloxy)-5,7-dihydroxy-4-oxo-4H-chromen-3-yl hydrogen sulfate	0.49347	-1.019	0.048578	1.3136
N-[(3-Hydroxy-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl)carbamoyl]-4-methylbenzenesulfonamide	0.49386	-1.0178	0.014335	1.8436
PFUnDA	0.49492	-1.0147	0.015565	1.8079
<b>Higher</b>				
.	2.0329	1.0236	0.0047607	2.3223
shrimp shell	2.0559	1.0398	0.0003514	3.4542
5-Methyl-1-(1,3,5-trimethyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole	2.0614	1.0436	0.0056697	2.2464
ML-236C	2.0692	1.0491	0.033437	1.4758
9-Phenylnonanoic acid	2.0822	1.0581	0.0098593	2.0062
DL-Mandelic acid	2.0829	1.0586	0.012684	1.8968
Guaifenesin	2.0989	1.0696	0.015754	1.8026
(11Z)-eicoseneoylcarnitine	2.0996	1.0701	0.041975	1.377
Prostaglandin F1 Alcohol	2.1015	1.0714	0.012072	1.9182
Tauropine	2.1305	1.0912	0.016397	1.7852
dacisteine	2.1343	1.0938	0.0063144	2.1997
glutaral	2.1406	1.098	0.01449	1.8389
Formiminoglutamic Acid	2.1903	1.1311	0.032321	1.4905
4-Hydroxynonenal	2.2045	1.1404	0.014487	1.839
7-hydroxy Pestalotin	2.2252	1.1539	6.13E-05	4.2127
Acetyl-L-carnitine	2.2328	1.1589	0.020751	1.683
C2 Dihydroceramide	2.235	1.1603	0.00030488	3.5159
Zolmitriptan	2.2442	1.1662	0.036964	1.4322
Nicotinyl methylamide	2.3014	1.2025	0.00092897	3.032
13(S)-HOTrE	2.3016	1.2026	0.043142	1.3651
3-Hydroxybutyric acid	2.3326	1.2219	0.0036976	2.4321
Ethyl sulfate	2.3476	1.2312	0.026543	1.5761
Idrocilamide	2.3489	1.232	0.0022937	2.6395
DOG	2.3518	1.2338	0.0015267	2.8162
bhas#24	2.4055	1.2663	0.022517	1.6475
Saccharin	2.4269	1.2791	0.0041211	2.385
(11Z,14Z)-eicosadienoylcarnitine	2.4531	1.2946	0.0033275	2.4779
MFCD08277025	2.4569	1.2968	0.029725	1.5269
[Similar to: 17-AAG; _Mass: -2.0472 Da]	2.4866	1.3142	0.011474	1.9403
2-(((2S,3R)-2-Methyl-3-pentadecyl-2-oxiranyl)carbonyl)amino)propyl acetate	2.5229	1.3351	0.018922	1.723

6beta-(Dimethylamino)-3beta,5-dihydroxy-5alpha-pregnan-20-one	2.5466	1.3486	0.014183	1.8482
(S)-N-Boc-L-homoserine ethyl ester	2.5662	1.3597	0.0035054	2.4553
Fesoterodine	2.6145	1.3865	0.0097098	2.0128
4149853	2.6191	1.3891	0.039759	1.4006
MFCD22416941	2.6342	1.3973	0.01032	1.9863
(2E)-hexadecenoylcarnitine	2.6379	1.3994	0.024175	1.6166
Pirimicarb	2.6407	1.4009	0.018743	1.7272
Lumula	2.6711	1.4174	0.010546	1.9769
7309670	2.6902	1.4277	0.0053487	2.2717
[Similar to: 2-benzylideneindan-1-one; _Mass: 60.0998 Da]	2.7152	1.4411	0.0015824	2.8007
C6 ceramide	2.7257	1.4466	3.27E-05	4.4856
Atagabalin	2.7303	1.4491	0.0063632	2.1963
5-Octyl D-glutamate	2.8141	1.4927	0.020602	1.6861
CERAMIDE 4	2.8454	1.5086	0.00049041	3.3094
(5S,9R)-12-[(2R)-6-Hydroxy-2,5,7,8-tetramethyl-3,4-dihydro-2H-chromen-2-yl]-5,9-dimethyldodecanoic acid	2.8501	1.511	0.0042721	2.3694
N-Palmitoyl-L-methionine	2.881	1.5266	0.0011582	2.9362
N-Butyl-1H-pyrazolo[3,4-d]pyrimidin-4-amine	2.9437	1.5576	0.010568	1.976
C2-ceramide	2.9467	1.5591	0.00042046	3.3763
625	3.0295	1.5991	0.0011364	2.9445
(2E)-N-[(3S)-2-Oxotetrahydro-3-furanyl]-2-dodecenamide	3.0489	1.6083	0.036512	1.4376
L-Propargylglycine	3.0529	1.6102	0.038065	1.4195
[Similar to: 2-benzylideneindan-1-one; _Mass: 174.8359 Da]	3.0682	1.6174	0.025036	1.6014
N-[(4Z,7Z,10Z,13Z,16Z,19Z)-docosahexaenoyl]-L-glutamic acid	3.0792	1.6226	0.012576	1.9005
Nikethamide	3.1083	1.6361	0.0022363	2.6505
asn-arg	3.1121	1.6379	0.00011809	3.9278
(2a'R,3R,3'R,5R,5'R,6a'S,9a'R)-5-(3-Furyl)-3'-hydroxy-9a'-(hydroxymethyl)-5'-methyloctahydro-3'H,6a'H-spiro[furan-3,6'-naphtho[1,8a-b]oxet]-2-one	3.2534	1.7019	0.048492	1.3143
Medrogestone	3.2605	1.7051	8.72E-05	4.0593
Crotanecine	3.3064	1.7252	0.0234	1.6308
3-Methylazelaic acid	3.4129	1.771	0.01979	1.7036
Palmitoylcarnitine	3.4325	1.7793	0.0016543	2.7814
8-{3-[(2E)-1-Hydroxy-2-octen-1-yl]-2-oxiranyl}octanoic acid	3.4424	1.7834	0.0035375	2.4513
3-Hydroxysebacic acid	3.5303	1.8198	0.0049285	2.3073
talernol	3.6109	1.8524	0.04301	1.3664
Hydroxypropionylcarnitine	3.6253	1.8581	0.00043259	3.3639
methyl-2-pyrimidinepropanoic acid	3.7562	1.9093	0.015877	1.7992



(2R)-3-[(Hydroxy{[(2S,3R,5S,6S)-3,4,5-trihydroxy-2,6-bis(alpha-D-mannopyranosyloxy)cyclohexyl]oxy}phosphoryl)oxy]-2-[(9Z)-9-octadecenoyloxy]propyl nonadecanoate	3.7985	1.9254	0.041136	1.3858
3-Hydroxy-N-[(3S)-2-oxotetrahydro-3-furanyl]octanamide	3.8125	1.9307	2.69E-05	4.5707
N1-(1,3,5-Trimethyl-1H-pyrazol-4-yl)-2-cyano-3-(dimethylamino)acrylamide	3.8173	1.9325	0.00040707	3.3903
(+)-Australine	3.8285	1.9368	0.0079083	2.1019
Taurocholic Acid 3-sulfate	3.8499	1.9448	0.0013549	2.8681
Biotin-azide	4.2303	2.0808	0.00039168	3.4071
(1S,4S,4aR,8aS)-4-[(3S)-3-Hydroxy-3-methyl-4-penten-1-yl]-4a,8,8-trimethyl-3-methylenedecahydro-1-naphthalenyl acetate	4.2674	2.0934	5.09E-07	6.293
[Similar to: 2-benzylideneindan-1-one; _Mass: 4.0749 Da]	4.2779	2.0969	4.10E-05	4.3868
2-Aminoethyl (2S,3R,4E,6E)-3-hydroxy-2-[(2-hydroxyoctadecanoyl)amino]-4,6-pentadecadien-1-yl hydrogen phosphate	4.288	2.1003	0.039138	1.4074
(9Z,12Z,15Z)-3-hydroxyoctadecatrienoylcarnitine	4.5284	2.179	0.025658	1.5908
Isococculidine	4.7683	2.2535	9.83E-05	4.0073
Heptadecanoic Acid	4.7736	2.2551	3.43E-05	4.4647
2'-Deoxyinosine	4.8061	2.2649	1.96E-05	4.708
EN0350000	5.2879	2.4027	0.0049175	2.3083
Dobutamine	5.3549	2.4209	0.0017343	2.7609
Isoprenaline	6.0931	2.6072	1.16E-05	4.9342
Pheneturide	6.1299	2.6159	0.0081558	2.0885
Xanthurenic acid	6.3046	2.6564	0.00039193	3.4068
Propionylcarnitine	6.3256	2.6612	0.00022785	3.6424
N-(2-Cyanoethyl)-L-glutamine	8.5683	3.099	0.0040603	2.3914

**Table S5.** Untargeted metabolomic analysis in liver tissue of mice exposed to polystyrene (2mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S5.

**Table S6.**

Untargeted Metabolomic Analysis in Liver Tissue of Mice Exposed to Polystyrene (4mg/week) p = 0.05	FC	log2(FC)	raw.pval	-LOG10(p)
<b>Lower</b>				
DL-2,6-Diaminopimelic acid	0.26133	-1.936	0.0015852	2.7999
pro-trp	0.28358	-1.8182	0.0010486	2.9794
pro-met	0.30892	-1.6947	0.013482	1.8703
2-methylcitric acid	0.32055	-1.6414	0.043605	1.3605
Aceglutamide	0.32914	-1.6032	0.021286	1.6719
2-[2-oxo-2-(pyridin-3-ylamino)ethoxy]acetic acid	0.34693	-1.5273	0.015856	1.7998
5,6-Dihydroxy-3-methyl-2(1H)-quinolinone	0.37386	-1.4194	0.014026	1.8531
(8Z,11Z,14Z)-Heptadecatrienal	0.37674	-1.4084	0.034502	1.4622
meprobamate	0.38727	-1.3686	0.0058311	2.2342
(2S,3R,5S)-3-(2-Aminoethyl)-7-oxo-4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylic acid	0.40367	-1.3088	0.0018036	2.7439
PESTALOTIN	0.40632	-1.2993	0.0094446	2.0248
N-acetyl-beta-D-glucosaminyllamine	0.41155	-1.2809	0.0042603	2.3706
MFCD00025555	0.41371	-1.2733	0.001205	2.919
PKF118-310	0.42604	-1.231	0.0094004	2.0269
Threonylglutamine	0.43955	-1.1859	0.0023435	2.6301
Ectoine	0.44391	-1.1717	0.0035884	2.4451
methocarbamol	0.44418	-1.1708	0.00763	2.1175
UAMC-3203	0.44539	-1.1668	0.0008196 6	3.0864
thr-arg	0.44598	-1.165	0.0072448	2.14
Glycylnorvaline	0.44703	-1.1616	0.0037748	2.4231
Lacinilene C 7-methyl ether	0.4502	-1.1514	0.016636	1.7789
N-Acetyl-D-alloisoleucine	0.45347	-1.1409	0.004781	2.3205
[Similar to: Xanthosine; _Mass: 35.9766 Da]	0.4561	-1.1326	0.0044703	2.3497
ALA-GLU	0.45634	-1.1318	0.030628	1.5139
ser-arg	0.45946	-1.122	0.0048375	2.3154
(15Z,19R)-25-Amino-22-hydroxy-22-oxido-17,21,23-trioxa-22lambda~5~-phosphapentacos-15-en-19-yl (9Z)-9-pentadecenoate	0.46003	-1.1202	0.013034	1.8849
LysoPC(22:5(7Z,10Z,13Z,16Z,19Z))	0.46142	-1.1158	0.017241	1.7634
N-Acetyl-L-glutamine	0.46587	-1.102	0.041515	1.3818
pro-his	0.4766	-1.0692	0.010863	1.9641
Physovenine	0.48115	-1.0554	0.031185	1.5061
ser-gln	0.48451	-1.0454	0.0005229 5	3.2815
Leucylproline	0.49518	-1.014	0.0002496 9	3.6026
<b>Higher</b>				
Idrocilamide	2.0058	1.0042	0.0092144	2.0355
7309670	2.01	1.0072	0.031327	1.5041

2-Aminoethyl (2S,3R,4E,6E)-3-hydroxy-2-[(2-hydroxyoctadecanoyl)amino]-4,6-pentadecadien-1-yl hydrogen phosphate	2.16	1.111	0.039314	1.4055
{[5-[(2S)-2-Carboxy-2-(trimethylammonio)ethyl]-1H-imidazol-2-yl]sulfanyl}oxidanide	2.2238	1.153	0.0003359 1	3.4738
3-Hydroxybutyric acid	2.2579	1.175	0.015536	1.8087
2-Hydroxy-3-oxobutyl phosphate	2.6437	1.4026	0.033967	1.4689
methyl-2-pyrimidinepropanoic acid	2.6815	1.423	0.035126	1.4544
[Similar to: 2-benzylideneindan-1-one; _Mass: 4.0749 Da]	2.7045	1.4354	0.0035123	2.4544
N1-(1,3,5-Trimethyl-1H-pyrazol-4-yl)-2-cyano-3-(dimethylamino)acrylamide	2.7942	1.4824	0.034564	1.4614
Glyparamide	2.8295	1.5006	0.030294	1.5187
Heptadecanoic Acid	2.9187	1.5453	0.0018483	2.7332
Propionylcarnitine	3.0271	1.5979	0.0030375	2.5175
(5S,9R)-12-[(2R)-6-Hydroxy-2,5,7,8-tetramethyl-3,4-dihydro-2H-chromen-2-yl]-5,9-dimethyldodecanoic acid	3.0475	1.6076	0.012462	1.9044
625	3.0902	1.6277	0.01578	1.8019
N-[(4Z,7Z,10Z,13Z,16Z,19Z)-docosahexaenoyl]-L-glutamic acid	3.1346	1.6483	0.033176	1.4792
trimethadione	3.3756	1.7551	0.047143	1.3266
.alpha.-Aminoadipic acid	3.5751	1.838	0.03421	1.4658
C8-HSL	3.5762	1.8384	0.030898	1.5101
g-Glutamylcysteine	3.7182	1.8946	0.02835	1.5474
_Glutamylcysteine	3.7317	1.8998	0.010297	1.9873
[Similar to: 17-AAG; _Mass: -2.0472 Da]	3.732	1.8999	0.039677	1.4015
N-(2-Cyanoethyl)-L-glutamine	3.8174	1.9326	0.020004	1.6989
2-Aminoadipic acid	3.9862	1.995	0.022671	1.6445
6-Oxo-pipecolinic acid	4.2361	2.0827	0.014026	1.8531
4-Pyridoxic acid	4.2507	2.0877	0.013754	1.8616
			0.0002200	
Biotin-azide	4.4478	2.1531	4	3.6575
Taurocholic Acid 3-sulfate	7.0675	2.8212	0.018604	1.7304

**Table S6.** Untargeted metabolomic analysis in liver tissue of mice exposed to polystyrene (4mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S6.

**Table S7.**

<b>Untargeted Metabolomic Analysis in Liver Tissue of Mice Exposed to Mixed Polymer (2mg/week) p = 0.05</b>	<b>FC</b>	<b>log2(FC)</b>	<b>raw.pval</b>	<b>-LOG10(p)</b>
<b>Lower</b>				
Palmitonitrile	0.021396	-5.5465	0.0030121	2.5211
3-Nonyl-1H-pyrazole	0.10022	-3.3187	0.01055	1.9767
2-Amino-1,3,4-octadecanetriol	0.1105	-3.1779	0.0035181	2.4537
Cinnassiol C3	0.11617	-3.1057	0.0026471	2.5772
Arachidoyl Ethanolamide	0.12978	-2.9459	0.0078264	2.1064
NP-019401	0.14679	-2.7682	0.0060957	2.215
sphinganine	0.21485	-2.2186	0.0021704	2.6635
(E)-9-Isopropyl-6-methyl-5,9-decadiene-2-one	0.22925	-2.125	0.0012675	2.8971
Tridemorph	0.24417	-2.0341	0.049473	1.3056
C20 sphinganine	0.24417	-2.0341	0.049473	1.3056
FF-MAS	0.25584	-1.9667	0.001591	2.7983
RG3715000	0.25658	-1.9625	0.018146	1.7412
Solacapine	0.25965	-1.9453	0.01571	1.8038
1-Oxo-1H-isochromene-3-carbaldehyde	0.26269	-1.9285	0.0046897	2.3289
2444643W XK	0.27402	-1.8676	0.0085275	2.0692
Phlegmarine	0.279	-1.8417	0.00095641	3.0194
7-ketodeoxycholic acid	0.30457	-1.7151	0.048309	1.316
6-(Methylthio)purine	0.30839	-1.6972	0.0020384	2.6907
phomalactone	0.32206	-1.6346	0.049065	1.3092
L-Aspartic acid	0.3224	-1.6331	0.018845	1.7248
Serratanidine	0.3252	-1.6206	0.0045603	2.341
Gabapentin related compound E	0.33726	-1.5681	0.0030868	2.5105
8-[(3,3-Dimethyl-2-oxiranyl)methyl]-7-methoxy-2H-chromen-2-one	0.34118	-1.5514	0.047497	1.3233
N-[(9Z)-3-Hydroxy-9-octadecenoyl]glycine	0.36635	-1.4487	0.0018601	2.7305
Ergosterol	0.37159	-1.4282	0.0027581	2.5594
Dichloroacetic acid	0.38258	-1.3862	0.0029536	2.5296
spisulosine	0.39101	-1.3547	0.0022003	2.6575
Diglyme	0.39443	-1.3422	0.0036312	2.44
3222	0.39667	-1.334	0.047353	1.3246
N-tetradecanoyl-4-hydroxysphinganine	0.40625	-1.2996	0.0021039	2.677
Thalictroidine	0.41129	-1.2818	0.0025662	2.5907
Lauramide	0.41128	-1.2818	0.0039111	2.4077
Camylofin	0.41557	-1.2668	0.011212	1.9503
1,2-Cyclohexanediol	0.42247	-1.2431	0.0065401	2.1844
Glutaryl carnitine	0.42568	-1.2322	0.0018071	2.743
all-trans-7-hydroxyhexadeca-2,4,8,10-tetraenoic acid	0.43437	-1.203	0.01017	1.9927
MFC00674434	0.45938	-1.1223	0.043783	1.3587
Valpromide	0.46996	-1.0894	0.0064414	2.191

(2E)-2-Octenal	0.46996	-1.0894	0.0064414	2.191
Myristoleyl alcohol	0.4744	-1.0758	0.0044952	2.3473
17-amino-5 $\beta$ -androstan-11-ol	0.47514	-1.0736	0.0030353	2.5178
Tapentadol	0.47523	-1.0733	0.00060202	3.2204
Capsi-amide	0.47963	-1.06	0.0075999	2.1192
Sphingosine (d18:1(14Z))	0.48411	-1.0466	0.045884	1.3383
MFCD00002821	0.48411	-1.0466	0.045884	1.3383
2-[4-(3-Hydroxypropyl)-2-methoxyphenoxy]-1,3-propanediol	0.48477	-1.0446	0.003224	2.4916
Methyl (11E)-8-hydroxy-11,17-octadecadien-9-ynoate	0.48629	-1.0401	0.027321	1.5635
1-Phenethyl-4-piperidone	0.48799	-1.0351	0.0014345	2.8433
N-(9-oxodecyl)acetamide	0.48799	-1.0351	0.0014345	2.8433
O-adipoylcarnitine	0.49934	-1.0019	0.02783	1.5555
<b>Higher</b>				
RG5927903	2.0069	1.0049	0.013412	1.8725
13-deoxytedanolide	2.0592	1.0421	0.0088788	2.0516
N-methylmorphinan	2.0742	1.0525	0.0053266	2.2735
Panthenol	2.0855	1.0604	0.012243	1.9121
[Similar to: 7-Oxobenz[de]anthracene; _Mass: -7.9880 Da]	2.1012	1.0712	0.031935	1.4957
Gly-Ile	2.1456	1.1014	0.024153	1.617
PCHP	2.1477	1.1028	0.0051854	2.2852
Oxohongdenafil	2.1801	1.1244	0.0043332	2.3632
(9S,12R)-9,12-Dihydroxy-10-hexadecynoic acid	2.1894	1.1306	0.0078527	2.105
3-Methylundecanoic acid	2.1976	1.1359	0.010272	1.9883
(9Z)-N-[(2S,3R,4E,6E)-1,3-Dihydroxy-4,6-tetradecadien-2-yl]-2-hydroxy-9-octadecenamamide	2.2041	1.1402	0.010636	1.9732
PEG n15	2.2121	1.1454	0.009133	2.0394
N <sup>6</sup> -Tetradecanoyl-L-lysine	2.2206	1.1509	0.03223	1.4917
Netilmicin	2.231	1.1577	0.005635	2.2491
Succinic acid	2.2491	1.1694	0.00081137	3.0908
NP-017710	2.2752	1.186	0.0096522	2.0154
PEG n16	2.2974	1.2	0.0068627	2.1635
Nifenazone	2.3244	1.2169	0.0073105	2.1361
Diacetoxyscirpenol	2.3673	1.2432	0.0070996	2.1488
(1S,4R,7S,9R)-9-Methyl-8-azatetracyclo[5.5.3.0 <sup>1,8</sup> .0 <sup>4,9</sup> ]pentadec-5-ene	2.3826	1.2525	0.0049059	2.3093
PEG n13	2.3902	1.2571	0.0052044	2.2836
PEG n12	2.4062	1.2667	0.0050144	2.2998
Microcystin-LA	2.4757	1.3079	0.0039341	2.4052
PEG n14	2.4792	1.3099	0.0046633	2.3313
1-(2-Phenyl-2-propanyl)piperidine	2.4902	1.3163	0.0050035	2.3007

nicosulfuron [ANSI]	2.4971	1.3202	0.0037391	2.4272
Imatinib	2.5825	1.3687	0.0043963	2.3569
miglustat	2.5907	1.3734	0.0024378	2.613
capuride	2.5973	1.377	0.045614	1.3409
NP-014287	2.6117	1.385	0.027934	1.5539
{{(3R,4S)-1-(Phenylacetyl)-3-[2-(4-phenyl-1-piperazinyl)ethyl]-4-piperidinyl}acetic acid	2.638	1.3994	0.004281	2.3685
Cassaidine	2.6461	1.4039	0.0055312	2.2572
O-pentadecanoylcarnitine	2.6461	1.4039	0.0055312	2.2572
Arachidonoyl ethanolamide phosphate	2.6489	1.4054	0.0044945	2.3473
(1R,9S)-11-(1-Acetyl-4-piperidinyl)-5-(2-methylphenyl)-7,11-diazatricyclo[7.3.1.0 <sub>2,7</sub> ]trideca-2,4-dien-6-one	2.6638	1.4135	0.0047276	2.3254
2-(4,4-diphenyl-1-piperidinobuta-1,3-dienyl)phenyl acetate	2.719	1.4431	0.0038723	2.412
Tropicamide	3.5057	1.8097	0.012837	1.8915
Nicotinuric acid	4.0448	2.0161	0.042366	1.373
(1R,3S,5Z)-5-{{(2E)-2-[(1Z,3aS,7aS)-1-(6-Ethyl-6-hydroxy-3-octyn-2-ylidene)-7a-methyloctahydro-4H-inden-4-ylidene]ethylidene}-4-methylene-1,3-cyclohexanediol	4.0919	2.0328	0.04633	1.3341
1-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-8-methyl-1,2,3,4-tetrahydroquinoline	4.8108	2.2663	0.044811	1.3486
4-(Hydroxymethyl)benzenesulfonic acid	4.8158	2.2678	0.0019788	2.7036
(2E)-N-[(3S)-2-Oxotetrahydro-3-furanyl]-2-dodecenamide	5.6221	2.4911	0.014135	1.8497
(5Z,8Z,11Z,14Z)-N-(4-Sulfamoylphenyl)-5,8,11,14-icosatetraenamide	5.8275	2.5429	0.023257	1.6335



**Table S7.** Untargeted metabolomic analysis in liver tissue of mice exposed to mixed polymer (2mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S7.

**Table S8.**

<b>Untargeted Metabolomic Analysis in Liver Tissue of Mice Exposed to Mixed Polymer (4mg/week) p = 0.05</b>	<b>FC</b>	<b>log2(FC)</b>	<b>raw.pval</b>	<b>-LOG10(p)</b>
<b>Lower</b>				
Palmitonitrile	0.019556	-5.6763	0.0023256	2.6335
Cinnassiol C3	0.075638	-3.7247	0.00072344	3.1406
3-Nonyl-1H-pyrazole	0.092625	-3.4324	0.0081441	2.0892
Arachidoyl Ethanolamide	0.094228	-3.4077	0.0021178	2.6741
2-Amino-1,3,4-octadecanetriol	0.12039	-3.0542	0.0050234	2.299
NP-019401	0.13125	-2.9296	0.004194	2.3774
Tridemorph	0.16251	-2.6214	0.0066947	2.1743
C20 sphinganine	0.16251	-2.6214	0.0066947	2.1743
sphinganine	0.20631	-2.2771	0.0020385	2.6907
(E)-9-Isopropyl-6-methyl-5,9-decadiene-2-one	0.23376	-2.0969	0.0030405	2.5171
5-phenyl-N,N-bis(2-pyridinylmethyl)-1,3-oxazole-4-carboxamide	0.23878	-2.0663	0.00043888	3.3577
N-[(3E)-2-Hydroxy-3-octenoyl]glycine	0.24862	-2.008	0.0019758	2.7043
3222	0.25044	-1.9975	0.0046931	2.3285
2444643W XK	0.25671	-1.9618	0.0058224	2.2349
5-Methoxyindole	0.25795	-1.9549	0.028846	1.5399
2,2'-Iminodipropan-1-ol	0.26357	-1.9237	0.00066543	3.1769
1-Oxo-1H-isochromene-3-carbaldehyde	0.27058	-1.8859	0.0059783	2.2234
Solacapine	0.27383	-1.8686	0.02078	1.6824
Gabapentin related compound E	0.27762	-1.8488	0.00079405	3.1002
7-ketodeoxycholic acid	0.27975	-1.8378	0.035502	1.4497
6-(Methylthio)purine	0.28534	-1.8093	0.0007583	3.1202
Serratanidine	0.30958	-1.6916	0.0033343	2.477
FF-MAS	0.31689	-1.6579	0.0077509	2.1106
Phlegmarine	0.32295	-1.6306	0.0012372	2.9076
FG7175000	0.32419	-1.6251	0.017843	1.7485
8-[(3,3-Dimethyl-2-oxiranyl)methyl]-7-methoxy-2H-chromen-2-one	0.34296	-1.5439	0.048037	1.3184
[Similar to: 1-ethyl 4-(2-oxo-1,2-diphenylethyl) succinate; _Mass: -152.2363 Da]	0.36461	-1.4556	0.0089337	2.049
Dichloroacetic acid	0.36614	-1.4495	0.0027489	2.5608
Azelaic acid	0.39293	-1.3477	0.0013435	2.8718
Diglyme	0.39376	-1.3446	0.0037171	2.4298
dacisteine	0.39554	-1.3381	0.013211	1.8791
spisulosine	0.39751	-1.3309	0.0027051	2.5678
[Similar to: Ethyl-_-D-glucuronide; _Mass: -0.0364 Da]	0.40261	-1.3126	0.010686	1.9712
Glutaryl carnitine	0.41171	-1.2803	0.002303	2.6377
1,2-Cyclohexanediol	0.43139	-1.2129	0.0078425	2.1055

Lauramide	0.4322	-1.2102	0.0065226	2.1856
Ergosterol	0.43816	-1.1905	0.013593	1.8667
Stearamide	0.44405	-1.1712	0.0077637	2.1099
all-trans-7-hydroxyhexadeca-2,4,8,10-tetraenoic acid	0.4498	-1.1527	0.011339	1.9454
Thalictroidine	0.45221	-1.1449	0.0078041	2.1077
Valpromide	0.45268	-1.1434	0.0045605	2.341
(2E)-2-Octenal	0.45268	-1.1434	0.0045605	2.341
Gabapentin	0.45374	-1.1401	0.0081657	2.088
N-[(9Z)-3-Hydroxy-9-octadecenoyl]glycine	0.45421	-1.1386	0.0080892	2.0921
N-nonanoyl-L-Homoserine lactone	0.45546	-1.1346	0.0052358	2.281
N-tetradecanoyl-4-hydroxysphinganine	0.4595	-1.1219	0.0089212	2.0496
MFCD00674434	0.46155	-1.1154	0.038871	1.4104
Bis(2-ethylhexyl) amine	0.4647	-1.1056	0.004417	2.3549
Methyl (11E)-8-hydroxy-11,17-octadecadien-9-ynoate	0.46768	-1.0964	0.00556	2.2549
2-[4-(3-Hydroxypropyl)-2-methoxyphenoxy]-1,3-propanediol	0.47374	-1.0778	0.0026761	2.5725
Camylofin	0.47936	-1.0608	0.030489	1.5159
13(S)-HODE methyl ester	0.47954	-1.0603	0.045993	1.3373
Timonacic	0.47996	-1.059	0.03092	1.5098
Bialaphos	0.48075	-1.0566	0.018	1.7447
Capsi-amide	0.49059	-1.0274	0.0095741	2.0189
N-Acetylalanine	0.49396	-1.0175	0.00036871	3.4333
C17 Sphingosine	0.49836	-1.0048	0.00024685	3.6076
dimethylformamide	0.4989	-1.0032	0.011518	1.9386
<b>Higher</b>				
Zalcitabine	2.1559	1.1083	0.022836	1.6414
methyl 8-[2-(2-formyl-vinyl)-3-hydroxy-5-oxo-cyclopentyl]-octanoate	2.1587	1.1102	0.0030167	2.5205
(9Z)-N-[(2S,3R,4E,6E)-1,3-Dihydroxy-4,6-tetradecadien-2-yl]-2-hydroxy-9-octadecenamamide	2.1711	1.1184	0.032642	1.4862
(+)-Corydaline	2.1738	1.1202	0.005373	2.2698
2-methoxy-17beta-estradiol 3-sulfate	2.1768	1.1222	0.005917	2.2279
N-methylmorphinan	2.1779	1.1229	0.0044862	2.3481
13-deoxytedanolide	2.1879	1.1295	0.0073565	2.1333
3,3',5,5'-tetramethylbenzidine	2.1903	1.1311	0.0071517	2.1456
(2S,3S)-2,3-dihydro-3-hydroxyanthranilic acid zwitterion	2.1966	1.1353	0.038403	1.4156
1,3,3-Trimethyl-2-oxabicyclo[2.2.2]oct-6-yl hexopyranoside	2.236	1.161	0.048706	1.3124
4-[(Hydroxymethyl)(nitroso)amino]-1-(3-pyridinyl)-1-butanol	2.2517	1.171	0.0070161	2.1539
PCHP	2.2551	1.1732	0.004414	2.3552
Netilmicin	2.2551	1.1732	0.0061527	2.2109

Cassaidine	2.2884	1.1943	0.0077794	2.1091
O-pentadecanoylcarnitine	2.2884	1.1943	0.0077794	2.1091
5,5',6',9'-Tetrahydroxy-8,8'-dimethoxy-2,2'-dimethyl-4H,4'H-7,7'-bibenzo[g]chromene-4,4',6,9-tetrone	2.2957	1.199	0.040238	1.3954
PEG n13	2.34	1.2265	0.0056351	2.2491
PEG n12	2.3429	1.2283	0.0056901	2.2449
PEG n16	2.3618	1.2399	0.00559	2.2526
PEG n14	2.3835	1.2531	0.0053899	2.2684
RG5927903	2.3971	1.2613	0.0036752	2.4347
(1S,4R,7S,9R)-9-Methyl-8-azatetracyclo[5.5.3.0~1,8~.0~4,9~]pentadec-5-ene	2.4077	1.2677	0.0049653	2.3041
Indoxyl sulfate	2.4149	1.272	0.014121	1.8501
Oxohongdenafil	2.4506	1.2932	0.0023974	2.6203
Uric acid	2.4817	1.3113	0.00044648	3.3502
naltrindole	2.547	1.3488	0.011466	1.9406
1-(2-Phenyl-2-propanyl)piperidine	2.5597	1.356	0.004667	2.331
nicosulfuron [ANSI]	2.573	1.3635	0.0029667	2.5277
NP-017710	2.5973	1.377	0.0037341	2.4278
CB5740000	2.6354	1.398	0.0097202	2.0123
8-(6-Carboxy-2,3,4-trihydroxyphenoxy)-3,4,9,10-tetrahydroxy-6-oxo-6H-benzo[c]chromene-1-carboxylic acid	2.6443	1.4029	0.0053627	2.2706
Succinic acid	2.6822	1.4234	0.0036719	2.4351
Diacetoxyscirpenol	2.7091	1.4378	0.0042251	2.3742
Nifenazone	2.7941	1.4824	0.0020854	2.6808
Microcystin-LA	2.8925	1.5323	0.0013246	2.8779
Tropicamide	2.9317	1.5517	0.013776	1.8609
(1R,9S)-11-(1-Acetyl-4-piperidinyl)-5-(2-methylphenyl)-7,11-diazatricyclo[7.3.1.02,7]trideca-2,4-dien-6-one	2.9978	1.5839	0.0036504	2.4377
Imatinib	3.0164	1.5928	0.0030885	2.5103
4-Formyl-2-methoxyphenyl hydrogen sulfate	3.1261	1.6444	0.0087616	2.0574
2-(4,4-diphenyl-1-piperidinobuta-1,3-dienyl)phenyl acetate	3.1698	1.6644	0.0023525	2.6285
{{(3R,4S)-1-(Phenylacetyl)-3-[2-(4-phenyl-1-piperazinyl)ethyl]-4-piperidinyl}acetic acid	3.2513	1.701	0.002696	2.5693
Arachidonoyl ethanolamide phosphate	3.3367	1.7384	0.0027297	2.5639
miglustat	3.3403	1.74	0.0061991	2.2077
4-Acetamidobenzoic acid	3.3822	1.758	0.032728	1.4851
GDC-0326	3.3911	1.7618	0.031017	1.5084
[Similar to: 7-Oxobenz[de]anthracene; _Mass: -7.9880 Da]	3.5088	1.811	0.037789	1.4226
Hippuric acid	3.5153	1.8137	0.027494	1.5608

guaiacol sulfate	3.8654	1.9506	0.030288	1.5187
Benzoic acid	3.8871	1.9587	0.025745	1.5893
(1R,3S,5Z)-5-{(2E)-2-[(1Z,3aS,7aS)-1-(6-Ethyl-6-hydroxy-3-octyn-2-ylidene)-7a-methyloctahydro-4H-inden-4-ylidene]ethylidene}-4-methylene-1,3-cyclohexanediol	3.9939	1.9978	0.042469	1.3719
Acetanilide	4.0117	2.0042	0.016723	1.7767
Victoria Pure Blue BO	4.216	2.0759	0.0054731	2.2618
2-Methylhippuric Acid	4.3662	2.1264	0.00062871	3.2016
(2E)-N-[(3S)-2-Oxotetrahydro-3-furanyl]-2-dodecenamide	4.7227	2.2396	0.0046099	2.3363
Iprovalicarb	4.7327	2.2427	0.024766	1.6061
6-Acetamido-2-oxohexanoic acid	5.2986	2.4056	0.036051	1.4431
(5Z,8Z,11Z,14Z)-N-(4-Sulfamoylphenyl)-5,8,11,14-icosatetraenamide	5.5231	2.4655	0.02353	1.6284
Nicotinic acid	14.498	3.8578	0.00024801	3.6055
4-(Hydroxymethyl)benzenesulfonic acid	23.537	4.5569	2.75E-05	4.5611

**Table S8.** Untargeted metabolomic analysis in liver tissue of mice exposed to mixed polymer (4mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S8.

**Table S9.**

<b>Untargeted Metabolomic Analysis in Brain Tissue of Mice Exposed to Polystyrene (2mg/week) p = 0.05</b>	<b>FC</b>	<b>log2(FC)</b>	<b>raw.pval</b>	<b>-LOG10(p)</b>
<b>Lower</b>				
MFCD00467154	0.18404	-2.4419	2.18E-05	4.662
N'-[(3Z)-1-(Cyclohexylmethyl)-2-oxo-1,2-dihydro-3H-indol-3-ylidene]benzohydrazide	0.20024	-2.3202	0.0041887	2.3779
3-Methoxytyramine	0.24779	-2.0128	0.0035842	2.4456
4-Anisic acid	0.37083	-1.4312	0.034659	1.4602
5-Hydroxy-2-furoic acid	0.4189	-1.2553	0.034717	1.4595
3-Amino-5-hydroxybenzoic acid	0.48286	-1.0503	0.0054427	2.2642
1581740	0.48373	-1.0477	9.91E-05	4.0037
Benzamidine	0.49396	-1.0175	0.022355	1.6506
<b>Higher</b>				
3,4-Dihydroxyphenylacetic acid	2.3187	1.2133	0.042961	1.3669
[Similar to: Sphingosine (d18:1); _Mass: -0.1092 Da]	2.4256	1.2783	0.046052	1.3368
5-({5-[(3,5-Dihydroxydecanoyl)oxy]-3-hydroxydecanoyl}oxy)-3-hydroxydecanoic acid	2.5454	1.3479	0.0179	1.7471
methypylon	2.6226	1.391	0.0038912	2.4099
Anapheline	3.2886	1.7175	0.019241	1.7158
(2S,3S)-2-hydroxytridecane-1,2,3-tricarboxylic acid	3.2895	1.7179	0.006238	2.205
3-({3-[(6-Deoxy-alpha-L-mannopyranosyl)oxy]undecanoyl}oxy)decanoic acid	4.6671	2.2225	0.0023429	2.6302

**Table S9.** Untargeted metabolomic analysis in brain tissue of mice exposed to polystyrene (2mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S9.



**Table S10.**

<b>Untargeted Metabolomic Analysis in Brain Tissue of Mice Exposed to Polystyrene (4mg/week) p = 0.05</b>	<b>FC</b>	<b>log2(FC)</b>	<b>raw.pval</b>	<b>-LOG10(p)</b>
<b>Lower</b>				
MFCD00467154	0.25061	-1.9965	0.00074465	3.128
3-Methoxytyramine	0.39271	-1.3485	0.03358	1.4739
<b>Higher</b>				
(2S)-2,3-Dihydroxypropyl (11Z)-11-icosenoate	2.0155	1.0112	0.042147	1.3752
N-Undecanoylglycine	2.1394	1.0972	0.027333	1.5633
N-Octanoyl-L-Homoserine lactone	2.1394	1.0972	0.027333	1.5633
Docosaenoyl Ethanolamide	2.1458	1.1015	0.0087426	2.0584
Allylacetone	2.1866	1.1287	0.042698	1.3696
Cyprodenate	2.1922	1.1324	0.021594	1.6657
(3E)-4-(4-Hydroxy-2,6,6-trimethyl-1-cyclohexen-1-yl)-3-buten-2-one	2.1942	1.1337	0.028693	1.5422
4-(2,6,6-Trimethylcyclohexa-1,3-dienyl)but-3-en-2-one	2.274	1.1852	0.026947	1.5695
Hexylbenzene	2.3129	1.2097	0.019185	1.717
1,4-Nonanediol diacetate	2.3146	1.2108	0.021878	1.66
Luciduline	2.3385	1.2256	0.0066151	2.1795
(4E)-4-Methyl-4-hexen-3-one	2.3679	1.2436	0.032756	1.4847
1,3,5-Heptatriene	2.3798	1.2508	0.032334	1.4903
2,4-OCTADIENAL	2.4868	1.3143	0.036462	1.4382
1,1,6-Trimethyl-1,2-dihydronaphthalene	2.504	1.3243	0.044919	1.3476
n-Amylbenzene	2.5142	1.3301	0.025391	1.5953
Guanethidine	2.5215	1.3343	0.013785	1.8606
(8S,17Z,28E,30R)-17,28-Dotriacontadiene-2,4,6,15,31-pentayne-1,8,30-triol	3.186	1.6718	0.029707	1.5271
[Similar to: Sphingosine (d18:1); _Mass: -0.1092 Da]	3.5539	1.8294	0.020307	1.6924

**Table S10.** Untargeted metabolomic analysis in brain tissue of mice exposed to polystyrene (4mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S10.

**Table S11.**

<b>Untargeted Metabolomic Analysis in Brain Tissue of Mice Exposed to Mixed Polymer (2mg/week) p = 0.05</b>	<b>FC</b>	<b>log2(FC)</b>	<b>raw.pval</b>	<b>-LOG10(p)</b>
<b>Lower</b>				
ACETYL PROLINE	0.41924	-1.2541	0.023976	1.6202
<b>Higher</b>				
9-Hexadecenoylcarnitine	2.0821	1.058	0.0087872	2.0562
Norisocorydine	2.497	1.3202	0.011574	1.9365
1,2,4-Butanetriol	2.6737	1.4189	0.045681	1.3403
beta-D-Ethyl glucuronide	2.8474	1.5097	0.0091114	2.0404
DL-Citrulline	4.1916	2.0675	0.020591	1.6863
2-O-methylcytosine	4.2073	2.0729	0.030687	1.513
Sulbactam	5.0679	2.3414	0.018464	1.7337
pp3	5.0915	2.3481	0.021432	1.6689
3-Hydroxy Darifenacin	5.2538	2.3934	0.041738	1.3795
[Similar to: 2-(4,4-diphenyl-1-piperidinobuta-1,3-dienyl)phenyl acetate; _Mass: -162.0873 Da]	5.4804	2.4543	0.030398	1.5172
Methylenediurea	5.721	2.5163	0.029217	1.5344
2-Amino-4-[(3-aminopropyl)amino]butanoic acid	13.555	3.7608	0.025114	1.6001

**Table S11.** Untargeted metabolomic analysis in brain tissue exposed to mixed polymer (2mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S11.

**Table S12.**

Untargeted Metabolomic Analysis in Brain Tissue of Mice Exposed to Mixed Polymer (4mg/week) p = 0.05	FC	log2(FC)	raw.pval	(-LOG10(p))
<b>Lower</b>				
[Similar to: Inosine-5'-monophosphate (IMP); _Mass: 0.0127 Da]	0.11073	-3.1749	0.00010683	3.9713
2-[(5-Nitro-1,3-thiazol-2-yl)carbamoyl]phenyl D-glucopyranosiduronic acid	0.1632	-2.6153	6.23E-05	4.2052
Acetyl-L-methionine	0.19238	-2.3779	0.017314	1.7616
HIAA	0.20711	-2.2715	0.029103	1.5361
Timonacic	0.2408	-2.0541	0.02149	1.6678
Goitrin	0.24427	-2.0335	0.027086	1.5672
S-Farnesyl Thioacetic Acid	0.24817	-2.0106	0.026264	1.5806
L-(-)-Methionine	0.30422	-1.7168	0.035337	1.4518
3-Methylsulfolene	0.30423	-1.7168	0.035365	1.4514
Sulfanilic acid	0.3064	-1.7065	0.027568	1.5596
3-(Sulfooxy)-L-tyrosine	0.33744	-1.5673	0.028539	1.5446
fMet	0.35441	-1.4965	0.03438	1.4637
Homocysteine thiolactone	0.35444	-1.4964	0.034461	1.4627
D-Glucopyranuronic acid	0.35816	-1.4813	0.013464	1.8708
e-Tokoferol	0.3602	-1.4731	0.017672	1.7527
[Similar to: 4-Dodecylbenzenesulfonic acid; _Mass: 98.0478 Da]	0.44889	-1.1556	0.0021113	2.6754
ACETYL PROLINE	0.45016	-1.1515	0.02704	1.568
D-Xylulosonic acid	0.48724	-1.0373	0.00015767	3.8022
<b>Higher</b>				
2-[3,5-Dihydroxy-4-(sulfooxy)phenyl]-5,7-dihydroxy-3,4-dihydro-2H-chromen-3-yl 3,4,5-trihydroxybenzoate	2.0225	1.0162	0.00074956	3.1252
ioprocecemic acid	2.0326	1.0233	0.0087689	2.0571
[Similar to: Inosine-5'-monophosphate (IMP); _Mass: 97.9767 Da]	2.0398	1.0284	0.0017951	2.7459
Caprolactam	2.059	1.0419	1.21E-05	4.9183
(2Z)-5-(1,2,4a,5-tetramethyl-7-oxo-1,2,3,4,4a,7,8,8a-octahydronaphthalen-1-yl)-3-methylpent-2-enoic acid	2.1267	1.0886	0.0039953	2.3985
methylguanidine	2.1453	1.1012	8.50E-05	4.0708
N-Methylisopelletierine	2.1893	1.1305	7.42E-05	4.1297
(2S,4S,6S,8S,10S,12R,14R,16R,18R)-19-Hydroxy-2,4,6,8,10,12,14,16,18-nonamethylhexatriacontanoic acid	2.2083	1.1429	0.0024868	2.6044
Dyphylline	2.229	1.1564	0.035645	1.448
Phenazone	2.4407	1.2873	0.010558	1.9764
Aliskiren	2.4422	1.2882	0.030334	1.5181

Cyano(3-phenoxyphenyl)methyl 2,2-dimethyl-3-(1,2,2,2-tetrabromoethyl)cyclopropanecarboxylate	2.4712	1.3052	0.015213	1.8178
MFCD00467154	2.4898	1.316	0.0047407	2.3242
Kukoamine A	2.566	1.3595	0.00092207	3.0352
DL-TYROSINE	2.7908	1.4807	0.0059852	2.2229
3,4-Dimethylbenzoic acid	2.8952	1.5337	0.020508	1.6881
Norisocorydine	2.8962	1.5342	0.0073437	2.1341
beta-D-Ethyl glucuronide	2.9459	1.5587	0.030876	1.5104
Sulbactam	3.1019	1.6331	0.018711	1.7279
Squalene	4.4364	2.1494	0.0013748	2.8618
HC Blue 1	4.5046	2.1714	0.039908	1.3989
9-Hexadecenoylcarnitine	5.0738	2.3431	0.017857	1.7482
2-amino-3-ketobutyric acid	5.8832	2.5566	0.033645	1.4731
2-O-methylcytosine	6.5839	2.7189	0.0253	1.5969
DL-Citrulline	6.8841	2.7833	0.0077373	2.1114
Methylenediurea	7.0728	2.8223	0.0010448	2.981
[Similar to: 2-(4,4-diphenyl-1-piperidinobuta-1,3-dienyl)phenyl acetate; _Mass: -162.0873 Da]	10.799	3.4328	0.00092639	3.0332
1-Nitrosopiperidine (NPIP)	17.03	4.09	0.022003	1.6575
2-Amino-4-[(3-aminopropyl)amino]butanoic acid	21.03	4.3944	0.00049211	3.3079

**Table S12.** Untargeted metabolomic analysis in brain tissue of mice exposed to mixed polymer (4mg/week);  $p = 0.05$ . Data can be found in supplemental Excel Table S12.

**Table S13.**

A. Targeted Metabolomics of Colon in Mice Exposed to Polystyrene (2mg/week)	FC	log2(FC)	raw.pval	-log10(p)
<b>Lower</b>				
Melatonin	0.13169	-2.9248	0.022623	1.6454
<b>Higher</b>				
5-Hydroxytryptophan	16.172	4.0154	0.021521	1.6671

B. Targeted Metabolomics of Colon in Mice Exposed to Polystyrene (4mg/week)	FC	log2(FC)	raw.pval	-log10(p)
<b>Higher</b>				
5-Hydroxytryptophan	43.173	5.4321	0.028309	1.5481



**Table S13.** Targeted Metabolomics of Colon in Mice Exposed to Polystyrene showing significantly altered metabolites for concentrations A) 2mg/week and B) 4mg/week.

Table S14.

A. Targeted Metabolomics of Colon in Mice Exposed to Mixed Polymer (2mg/week)	FC	log2(FC)	raw.pval	-log(10)p
<b>Lower</b>				
ADP ribose	0.051106	-4.2904	0.028892	1.5392
Nicotinamide	0.17804	-2.4898	0.0063979	2.194
<b>Higher</b>				
Melatonin	2.5207	1.3338	0.036607	1.4364
N'-Formylkynurenine	48.344	5.5953	0.026892	1.5704
Xanthurenic acid	91.706	6.5189	0.015512	1.8093
Kynurenic acid	435.75	8.7674	0.0042819	2.3684

B. Targeted Metabolomics of Colon in Mice Exposed to Mixed Polymer (4mg/week)	FC	log2(FC)	raw.pval	-log(10)p
<b>Lower</b>				
Indole	0.0038223	-8.0313	0.02725	1.5646
NICOTINIC ACID ADENINE DINUCLEOTIDE	0.082634	-3.5971	0.0086219	2.0644
Nicotinic acid	0.11305	-3.145	0.0094296	2.0255
NAD	0.14977	-2.7392	0.041662	1.3803
<b>Higher</b>				
Melatonin	3.1744	1.6665	0.032836	1.4836
N'-Formylkynurenine-†	39.422	5.3009	0.022044	1.6567
Xanthurenic acid	353.05	8.4637	0.026914	1.57
Kynurenic acid	859.43	9.7472	0.01023	1.9901

**Table S14.** Targeted Metabolomics of Colon in Mice Exposed to Mixed Polymer showing significantly altered metabolites for concentrations A) 2mg/week and B) 4mg/week.