

Supplementary Table SIX. Cochran's Q test and MR-Egger regression analysis for human blood metabolites and colorectal cancer risk (Data from Open GWAS database; The metabolites labeled red show heterogeneity or multivalidity)

Metabolites	Cochran's Q test		MR-Egger regression analysis	
	Q	P	Intercept	P
1-palmitoyl-2-arachidonoyl-gpc	30.34	0.45	-0.004	0.40
1,2-dipalmitoyl-gpc	17.23	0.90	0.002	0.81
1-palmitoyl-2-stearoyl-gpc (16:0/18:0)	28.59	0.64	-0.001	0.88
Arachidonate to linoleate ratio	28.75	0.19	-0.01	0.18
Retinol (Vitamin A) to linoleoyl-arachidonoyl-glycerol ratio	17.45	0.74	0.004	0.67
Arachidonate to oleate to vaccenate ratio	20.61	0.30	-0.01	0.10
1-oleoyl-2-linoleoyl-GPE	40.40	0.15	0.01	0.05
1-myristoyl-2-arachidonoyl-GPC (14:0/20:4)	40.87	0.01	-0.02	0.08
1-stearoyl-2-arachidonoyl-GPE (18:0/20:4)	40.62	0.07	-0.004	0.59
Imidazole lactate	22.19	0.77	-0.01	0.34
1-stearoyl-2-arachidonoyl-gpc (18:0/20:4)	48.63	0.05	-0.01	0.08
X-12731	18.50	0.86	0.01	0.25
Oleoyl-linoleoyl-glycerol to linoleoyl-arachidonoyl-glycerol ratio	34.76	0.07	0.02	0.01
Phosphate to linoleoyl-arachidonoyl-glycerol ratio	22.04	0.40	0.01	0.07
1-(1-enyl-palmitoyl)-GPC (p-16:0)	28.25	0.45	-0.02	0.02
Sphingadienine	19.61	0.36	0.01	0.33
1,2-dilinoleoyl-GPC (18:2/18:2)	28.01	0.03	0.02	0.08
X-18345	28.15	0.61	-0.01	0.33
1-(1-enyl-palmitoyl)-2-arachidonoyl- gpc (p-16:0/20:4)	65.98	0.002	-0.01	0.12
X-12822	9.43	0.93	0.01	0.37
X-25790	12.85	0.61	0.01	0.63
1-arachidonoyl-GPE (20:4n6)	55.61	0.02	-0.004	0.58
Creatine to carnitine ratio	14.66	0.74	0.003	0.81
3-carboxy-4-methyl-5-propyl-2-fura npropanoate (cmpf)	16.01	0.52	-0.002	0.91

1-(1-enyl-stearoyl)-2-linoleoyl-GPE (p-18:0/18:2)	36.45	0.01	0.02	0.19
Eicosapentaenoate (EPA; 20:5n3)	46.18	0.01	-0.01	0.32
Iminodiacetate (IDA)	13.90	0.61	0.01	0.49
1-(1-enyl-stearoyl)-2-arachidonoyl-G PE (p-18:0/20:4)	31.10	0.15	-0.03	0.001
Isovalerylcarnitine (C5)	25.84	0.47	0.01	0.37
Glutarylcarnitine (c5-dc)	38.82	0.19	0.002	0.84
Nonanoylcarnitine (C9)	20.07	0.52	0.0002	0.98
Oleoylcarnitine	17,17	0.88	-0.001	0.93
1-arachidonoyl-gpc (20:4n6)	42.65	0.04	-0.01	0.02
Serine to pyruvate ratio	10.92	0.93	-0.01	0.61
Adenosine 5'-monophosphate (AMP) to aspartate ratio	19.06	0.89	-0.003	0.78
Carnitine to ergothioneine ratio	26.42	0.15	-0.004	0.76
Phosphate to linoleoyl-arachidonoyl-glycerol ratio	35.94	0.07	0.02	0.02
Uridine to pseudouridine ratio	31.19	0.18	0.003	0.81
21-hydroxypregnenolone disulfate	37.72	0.44	-0.002	0.80
Linoleoyl-arachidonoyl-glycerol (18:2/20:4)	20.72	0.35	0.001	0.89
Retinol (Vitamin A) to linoleoyl-arachidonoyl-glycerol (18:2 to 20:4) ratio	33.34	0.10	0.03	0.002
Tartronate (hydroxymalonate)	18.18	0.51	0.002	0.87
X-11858	36.87	0.08	-0.02	0.13
Arachidonate (20:4n6)	42.79	0.04	-0.01	0.17
Sphingomyelin (d18:1/22:1, d18:2/22:0, d16:1/24:1)	32.72	0.04	0.01	0.71
1-palmitoyl-2-linoleoyl-gpc (16:0/18:2)	56.38	0.01	0.01	0.44
Glycosyl-N-behenoyl-sphingadienin e (d18:2/22:0)	34.38	0.16	-0.001	0.88
Spermidine to N-acetylputrescine ratio	14.92	0.87	0.01	0.54
Pyruvate to 3-methyl-2-oxobutyrate ratio	22.17	0.45	0.01	0.23
Arachidonate (20:4n6) to pyruvate ratio	31.51	0.01	-0.04	0.04
1-oleoyl-GPG (18:1)	21.13	0.78	-0.01	0.30

N2,n2-dimethylguanosine	8.08	0.95	-0.03	0.07
1-palmitoyl-2-linoleoyl-GPI (16:0/18:2)	43.51	0.01	0.01	0.64
N2,N5-diacetylornithine	31.61	0.21	-0.003	0.73
Adenosine 5'-diphosphate (ADP) to aspartate ratio	31.99	0.19	-0.01	0.41
X-18779	17.14	0.58	0.01	0.38
Oleoyl-linoleoyl-glycerol (18:1 to 18:2) to linoleoyl-arachidonoyl-glycerol (18:2 to 20:4) ratio	50.94	0.002	0.02	0.02
Hydroxyasparagine	26.10	0.20	0.004	0.74
1-oleoyl-2-docosaheptaenoyl-GPC (18:1/22:6)	33.67	0.29	0.01	0.34
X-23636	15.88	0.53	-0.01	0.67
X-12738	6.69	0.99	-0.003	0.83
N-lactoyl valine	11.58	0.71	-0.004	0.82
Betaine	17.55	0.86	-0.01	0.45
Heneicosapentaenoate (21:5n3)	11.75	0.76	-0.01	0.47
X-11381	7.82	1.00	-0.002	0.76
Lignoceroyl sphingomyelin (d18:1/24:0)	25.19	0.45	-0.01	0.61
X-12410	36.20	0.11	-0.01	0.37
4-acetamidobutanoate	12.93	0.80	0.003	0.67
X-23739	23.81	0.53	0.01	0.25
Adenosine 5'-diphosphate (ADP) to N-palmitoyl-sphingosine (d18:1 to 16:0) ratio	16.29	0.80	-0.004	0.67
Hexanoylcarnitine	29.28	0.14	0.001	0.91
N-acetyl leucine	18.17	0.38	0.01	0.56
1-arachidonylglycerol (20:4)	28.87	0.18	-0.02	0.07
Hydantoin-5-propionate	26.89	0.11	0.01	0.16
X-11852	18.14	0.87	-0.002	0.81
X-16580	10.50	0.84	0.01	0.48
Androstenediol (3beta,17beta) monosulfate	35.68	0.15	0.01	0.15
X-26054	53.61	0.01	0.002	0.76
Carnitine to propionylcarnitine ratio	18.23	0.63	0.01	0.22

1-(1-enyl-palmitoyl)-2-oleoyl-gpc (p-16:0/18:1)	49.79	0.003	0.01	0.44
Adenosine 5'-monophosphate (AMP) to EDTA ratio	9.93	0.77	-0.003	0.80
DHEAS	52.16	0.16	0.01	0.05
Docosatrienoate (22:3n6)	36.85	0.002	-0.02	0.34
Tetradecanedioate (C14-DC)	19.69	0.54	-0.004	0.49
Erucate (22:1n9)	26.37	0.09	-0.02	0.15
Methylsuccinoylcarnitine	27.98	0.57	0.01	0.35
Methylsuccinate	13.52	0.92	0.0001	0.99
X-23276	21.61	0.48	0.003	0.83
Andro steroid monosulfate C19H28O6S	34.28	0.64	-0.01	0.47
Deoxycholic acid glucuronide	22.20	0.68	0.01	0.40
X-13431	17.69	0.91	0.001	0.86
Alpha-hydroxyisovalerate	22.59	0.31	-0.003	0.78
Docosatrienoate (22:3n3)	19.62	0.55	-0.01	0.18
1-stearoyl-2-linoleoyl-gpc (18:0/18:2)	40.20	0.01	0.01	0.39
2-hydroxyhippurate (salicylurate)	24.36	0.44	0.01	0.51
Succinylcarnitine	27.80	0.47	0.02	0.01
N-acetylarginine	32.67	0.14	-0.01	0.41
X-14056	19.95	0.40	0.01	0.12
1-(1-enyl-palmitoyl)-2-linoleoyl-GP E (p-16:0/18:2)	38.38	0.01	0.01	0.52
Sphingomyelin (d18:0/18:0, d19:0/17:0)	31.45	0.39	0.01	0.50
1-methylxanthine	25.91	0.68	0.001	0.87
Picolinoylglycine	17.74	0.77	0.02	0.06
X-19141	28.92	0.18	-0.01	0.21
5-hydroxyindole sulfate	8.28	0.97	-0.01	0.52
X-13553	21.10	0.63	0.01	0.51
Cis-3,4-methyleneheptanoylcarnitine	20.26	0.63	-0.01	0.45
Homovanillate (hva)	18.49	0.73	-0.01	0.27
Hexadecenedioate (C16:1-DC)	27.92	0.67	0.003	0.53
1-palmitoyl-2-arachidonoyl-GPE (16:0/20:4)	34.95	0.01	0.003	0.78

Gamma-glutamylcitrulline	24.94	0.52	0.02	0.04
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