

Supplementary Table 1 The list of metabolites measured by the LC-MS/MS based targeted metabolomics platform.

In-house ID	Metabolite name	Linear calibration curve range (µmol/L)
M001	M001_Tryptophan	0.01 - 10
M002	M002_L-kynurenine	0.01 - 10
M003	M003_Serotonin	0.01 - 5
M004	M004_5-Hydroxyindoleacetic acid (5'-HIAA)	0.01 - 10
M005	M005_Kynurenic acid	0.01 - 1
M007	M007_cis-Aconitic acid	0.02 - 2
M008	M008_Succinic acid	0.5 - 5
M009	M009_Fumaric acid	0.5 - 10
M010	M010_Isocitric acid	0.1 - 5
M012	M012_L-malic acid	0.02 - 5
M013	M013_Succinyl coA	0.01 - 10
M015	M015_Acetyl coA	0.01 - 10
M016	M016_Oxoglutaric acid	0.1 - 10
M019	M019_Fructose 6-phosphate	0.01 - 2
M020	M020_Fructose 1,6-bisphosphate	0.02 - 0.5
M021	M021_2-Phosphoglyceric acid	0.01 - 10
M022	M022_Phosphoenolpyruvic acid	0.2 - 10
M023	M023_LValine	0.01 - 2
M024	M024_Leucine	0.01 - 1
M025	M025_Histidine	0.01 - 1
M026	M026_Phenylalanine	0.01 - 10
M027	M027_Glutamine	0.02 - 10
M028	M028_Tyrosine	0.01 - 10
M029	M029_Isoleucine	0.1 - 10
M030	M030_Threonine	0.05 - 1
M031	M031_Glutamic acid	0.02 - 2
M032	M032_Arginine	0.01 - 0.5
M033	M033_Lysine	0.02 - 0.5
M034	M034_S-Adenosylmethionine	0.02 - 2
M035	M035_Dihydroxyacetone phosphate	0.05 - 1
M036	M036_Picolinic acid	0.01 - 10
M038	M038_Palmitic acid	0.5 - 5
M039	M039_NADP	0.02 - 10
M041	M041_NAD	0.01 - 1
M043	M043_Dephospho-CoA	0.05 - 10
M046	M046_3-Hydroxy-3-methylglutaryl-CoA	0.01 - 10
M047	M047_Nicotinamide	0.01 - 10/5
M048	M048_AICA ribonucleotide	0.01 - 5
M049	M049_S-Adenosylhomocysteine	0.01 - 10
M050	M050_Deoxyribose 5-phosphate	0.01 - 2
M051	M051_Glucose 1-phosphate	0.01 - 2/0.5
M052	M052_dUMP	0.01 - 5
M054	M054_Hypoxanthine	0.01 - 2
M055	M055_D-ribose 5-phosphate	0.01 - 2
M056	M056_Glutathione	0.01 - 10
M057	M057_Gluconic acid	0.01 - 2
M058	M058_Uric acid	0.01 - 2
M062	M062_1-Methylhistidine	0.01 - 1
M063	M063_1-Methylnicotinamide	0.01 - 2
M064	M064_2,5-DHBA	0.2 - 10

M065	M065_Deoxycytidine	0.01 - 2
M068	M068_2-ketohexanoic acid	0.05 - 5
M069	M069_5-Methoxytryptophan	0.01 - 10
M070	M070_L-Acetylcarnitine	0.01 - 10
M071	M071_N-Alpha-acetyllysine	0.01 - 2
M073	M073_adenosine	0.01 - 1
M074	M074_Adenosine diphosphate ribose	0.01 - 10/2
M075	M075_ADP	0.01 - 2
M076	M076_Agmatine	0.02 -0.5
M077	M077_Aminoadipic acid	0.05 - 2
M078	M078_aminolevulinic acid	0.1 - 10
M079	M079_AMP	0.01 - 10
M080	M080_Biotin	0.01 - 10
M082	M082_Butyrylcholine	0.01 - 1
M083	M083_Carnitine	0.01 - 10/2
M084	M084_Chlorzoxazone	0.5 - 10
M085	M085_Citraconic acid	0.1 - 10
M086	M086_Citrulline	0.01 - 10
M087	M087_CMP	0.01 - 10
M089	M089_Cytosine	0.01 - 0.5
M090	M090_dAMP	0.01 - 10
M091	M091_Dehydroascorbic acid	0.5 - 5
M092	M092_Deoxyinosine	0.1 - 2
M093	M093_Deoxyuridine	0.1 - 10
M096	M096_2-Aminooctanoic acid	0.01 - 10
M097	M097_D-Glyceraldehyde 3-phosphate	0.05 - 2
M099	M099_FAD	0.01 - 10
M100	M100_Flavone	0.01 - 10
M101	M101_Folic acid	0.01 - 5/2
M103	M103_Gluconic acid	0.05 - 1
M105	M105_Glucosamine	0.02 - 2
M106	M106_Glucose 6-phosphate	0.01 - 2
M107	M107_Glucuronic acid	0.01 - 2
M108	M108_Glycerate	0.5 - 10
M109	M109_GMP	0.02 - 2 / 0.05 -10
M112	M112_Guanidoacetic acid	0.05 - 5
M113	M113_Guanine	0.01 - 10
M114	M114_Guanosine	0.01 - 10
M117	M117_Homoserine	0.01 - 5
M118	M118_Hydroxyisocaproic acid	0.01 - 10
M119	M119_Hydroxyphenylacetic acid	0.2 - 10
M121	M121_Imidazole	0.02 - 2
M122	M122_Imidazoleacetic acid	0.01 - 2
M123	M123_IMP	0.02 - 1
M124	M124_Indole	0.1 - 10
M125	M125_Indole-3-carboxylic acid	0.01 - 10
M126	M126_Indoleacrylic acid	0.01 - 10
M127	M127_lipoate	0.2 - 5
M128	M128_L-Pipecolic acid	0.02 - 5
M129	M129_Methionine sulfoxide	0.01 - 10
M131	M131_N-Acetyl-L-aspartic acid	0.01 - 2 / 0.02 - 1
M132	M132_N-Acetyl-D-glucosamine	0.01 - 1
M133	M133_N-Acetyl-L-alanine	0.02 - 10
M134	M134_N-acetylorcarnitine	0.01 - 5/2

M137	M137_Nicotinic acid	0.01 - 5/2
M138	M138_N-Methyl-D-aspartic acid	0.01 - 2 / 0.05 - 1
M139	M139_O-Acetyl-L-serine	0.1 - 2
M140	M140_Ornithine	0.01 - 0.5
M141	M141_Orotate	0.02 - 5
M142	M142_Oxaloacetate	0.02 - 10
M143	M143_Pantothenic acid	0.01 - 10
M144	M144_Perfluoroheptanoic acid	0.01 - 5
M145	M145_Phenyllactic acid	0.05 - 10
M146	M146_Phenylpropionic acid	0.05 - 10
M147	M147_Phenylpyruvate	0.1 - 10
M149	M149_4-Hydroxybenzoic acid	0.05 - 10
M150	M150_L-Proline	0.05 - 2
M151	M151_Purine	0.01 - 10
M152	M152_Pyridoxal 5'-phosphate	0.01 - 5
M153	M153_Pyridoxamine	0.01 - 0.5
M154	M154_Pyridoxine	0.01 - 1
M155	M155_Pyroglutamic acid	0.1 - 2
M157	M157_Flavin Mononucleotide	0.2 - 10
M158	M158_Shikimic acid	0.05 - 5
M160	M160_Sorbitol	0.1 - 5
M161	M161_Taurine	0.02 - 10
M162	M162_Thiamine	0.01 - 10
M163	M163_Thymidine	0.01 - 2/1
M164	M164_Thymine	0.01 - 10/5
M166	M166_Uridine diphosphate-N-acetylglucosamine	0.01 - 10
M167	M167_Uridine 5'-monophosphate	0.01 - 2
M168	M168_Uracil	0.01 - 10
M169	M169_Uridine	0.01 - 2
M170	M170_Xanthine	0.01 - 5
M171	M171_Xanthosine	0.01 - 5
M172	M172_Xanthylic acid	0.05 - 5
M173	M173_Xanthurenic acid	0.01 - 2
M174	M174_Adenosine triphosphate	0.05 - 5
M175	M175_Cytidine triphosphate	0.5 - 10
M176	M176_Guanosine triphosphate	0.05 - 5
M177	M177_Uridine triphosphate	0.02 - 5
M178	M178_dATP	0.01 - 10
M179	M179_dCTP	0.01 - 10
M180	M180_dGTP	0.05 - 2
M181	M181_dTTP	0.01 - 5
M182	M182_L-Cysteine	0.02/0.1 - 1
M183	M183_L-Alanine	0.5 - 10
M184	M184_L-Asparagine	0.1 - 10
M185	M185_Glycine	0.5 - 10
M186	M186_L-Aspartic acid	0.01 - 1
M187	M187_Argininosuccinic acid	0.01 - 2
M188	M188_Sarcosine	0.2 - 10
M190	M190_Betaine	0.05 - 5
M191	M191_Choline	0.01 - 1
M192	M192_Cystathionine	0.01 - 1
M194	M194_Urea	0.02 - 1
M195	M195_Cytidine	0.01 - 2
M196	M196_CDP	0.01 - 5

M197	M197_GDP	0.02 - 10
M198	M198_UDP	0.01 - 10
M200	M200_dCMP	0.01 - 2
M201	M201_dCDP	0.01 - 10
M202	M202_dGMP	0.05 - 10
M203	M203_dGDP	0.05 - 10
M204	M204_dTMP	0.01 - 5
M205	M205_dTDP	0.01 - 10
M206	M206_UDP- glucose	0.01 - 2
M207	M207_ADP-glucose	0.01 - 1
M211	M211_Maleic acid	0.1 - 10
M214	M214_Methylmalonic acid	0.1 - 2
M216	M216_2-Aminobenzoic acid	0.01 - 10
M217	M217_p-Aminobenzoic acid	0.01 - 10/5
M219	M219_2-Oxo-4-methylthiobutanoic acid	0.02 - 10
M220	M220_2-Pyrocatechuic acid	0.01 - 10
M221	M221_L-Dihydroorotic acid	0.01 - 2
M224	M224_4-Pyridoxic acid	0.01 - 1
M225	M225_2-keto-D-gluconic acid	0.01 - 2
M226	M226_D-Erythrose 4-phosphate	0.01 - 2
M227	M227_D-Glucaric acid	0.05 - 2
M228	M228_Inosine	0.01 - 2
M229	M229_D-Sedoheptulose 7-phosphate	0.01 - 2/1
M230	M230_N-Acetyl-glucosamine-1-phosphate	0.01 - 2
M231	M231_Cyclic AMP	0.01 - 10
M232	M232_Sucrose	0.01 - 5
M238	M238_Thiamine pyrophosphate	0.05 - 10
M239	M239_Adenosine phosphosulfate	0.01 - 10
M241	M241_Cholesterol sulfate	0.01 - 10
M242	M242_Citicoline	0.01 - 10
M243	M243_Taurodeoxycholic acid	0.01 - 2
M245	M245_Coenzyme A	0.1 - 10
M246	M246_Propionyl-CoA	0.01 - 10
M247	M247_3-Hydroxybutyryl-CoA	0.01 - 5
M248	M248_L-2-Hydroxyglutaric acid	0.01 - 2
M249	M249_Ethanlamine	0.01 - 1
M251	M251_Gamma-Aminobutyric acid	0.01 - 2
M254	M254_Creatinine	0.01 - 1
M255	M255_Creatine	0.01 - 1
M256	M256_N-Acetylputrescine	0.01 - 1
M257	M257_4-Hydroxyproline	0.02 - 5
M258	M258_Adenine	0.02 - 10
M259	M259_L-Homocysteine	0.05 - 2
M260	M260_L-Histidinol	0.01 - 1
M262	M262_Phosphorylcholine	0.02 - 1
M263	M263_Phosphoserine	0.5 - 10
M264	M264_N-Acetylglutamine	0.01 - 2
M265	M265_N-Acetylglutamic acid	0.01 - 5
M266	M266_Asymmetric dimethylarginine	0.01 - 2
M267	M267_L-Cystine	0.02 - 1
M268	M268_Deoxyadenosine	0.01 - 1
M269	M269_AICA-riboside	0.01 - 10
M271	M271_7-Methylguanosine	0.01 - 1
M272	M272_Beta-nicotinamide D-ribonucleotide	0.01 - 5

M273	M273_Riboflavin	0.01 - 10
M276	M276_3,5-Diiodothyronine	0.01 - 2
M277	M277_Putrescine	0.01 - 0.5
M278	M278_Spermidine	0.01 - 0.5
M279	M279_Spermine	0.01 - 1
M280	M280_Acetone	0.2 - 10
M281	M281_Alpha-Hydroxyisobutyric acid	0.01 -10
M282	M282_p-Hydroxyphenylacetic acid	0.01 -10
M289	M289_Dimethylamine	0.05 - 2
M290	M290_Glycocholic acid	0.01 - 10
M293	M293_Hippurate	0.01 - 10
M298	M298_Stigmasterol	0.01 - 10
M299	M299-Taurochenodesoxycholic acid	0.01 - 10
M300	M300_Taurocholic acid	0.01 - 10
M302	M302_Lithocholytaurine	0.01 - 10
M303	M303_Ursodeoxycholic acid	0.01 - 10
M304	M304_Campesterol	0.01 - 5
M305	M305_3-Phosphoglyceric acid	0.01 - 10
M306	M306_Thiamine monophosphate	0.01 - 10
M307	M307_Deoxyguanosine	0.01 - 10
M308	M308_Malonyl CoA	0.05 - 1
M309	M309_D-Phenyllactic acid	0.2 - 10
M310	M310_Citramalic acid	0.01 - 2
M311	M311_L-Homocysteic acid	0.01 - 2
M312	M312_Serine	0.02 - 10
M314	M314_CDP-ethanolamine	0.01 - 10
M315	M315_p-Cresyl sulfate	0.01 - 10
M316	M316_Lithocholic acid glycine conjugate	0.01 - 10
M317	M317_Dihydrothymine	0.01 - 0.2
M318	M318_ Alpha-N-Phenylacetyl-L-glutamine	0.01 - 10
M319	M319_ Phenylacetyl glycine	0.01 - 10
M327	M327_Lithocholic acid	0.01 -10
M328	M328_ Linoleyl Carnitine	0.01 -10
M329	M329_ Valerylcarnitine	0.01 -10
M330	M330_ Dodecanoylcarnitine	0.01 -10
M331	M331_ L-Palmitoylcarnitine	0.01 -10
M341	M341_ Tetradecanoylcarnitine	0.01 - 5
M342	M342_ Propionylcarnitine	0.01 - 10
M343	M343_ L-Octanoylcarnitine	0.01 - 10
M344	M344_ Decanoylcarnitine	0.01 - 5
M345	M345_ Malonyl carnitine	0.01 - 5
M346	M346_ Stearoylcarnitine	0.01 - 5

* Calibration standards are prepared in mass spectrometry grade water.

Supplementary Table 2 Significantly changed metabolites^a following 1.5-h intravenous infusion of irinotecan alone (on Cycle 1 Day 1)

Name	p-value	FDR	Pairwise Fisher's LSD post-hoc test										
			1-2	1-3	1-4	1-5	2-3	2-4	2-5	3-4	3-5	4-5	
N- α -acetyllysine	2.91E-05	0.004	■				■	■				■	■
Aminoadipic acid	3.29E-04	0.021		■				■	■			■	■
Asymmetric dimethylarginine	4.73E-04	0.021	■										
Thymine	9.09E-04	0.030	■										
Propionyl-L-carnitine	0.002	0.060			■			■	■			■	■
N-Acetylglutamic acid	0.003	0.063		■				■	■			■	■
L-Acetylcarnitine	0.004	0.063	■					■	■			■	■
Malonyl-L-carnitine	0.004	0.063	■					■	■			■	■
Cystathionine	0.005	0.063			■			■	■			■	■
Sorbitol	0.005	0.063	■					■	■			■	■
Creatine	0.005	0.063			■			■	■			■	■
L-Alanine	0.006	0.063	■					■	■			■	■
Uracil	0.006	0.065						■	■			■	■
Phenylalanine	0.010	0.098			■			■	■			■	■
D-Tryptophan	0.012	0.104			■			■	■			■	■
Imidazoleacetic acid	0.017	0.140		■				■	■			■	■
Arginine	0.019	0.142			■			■	■			■	■
Xanthine	0.020	0.142		■				■	■			■	■
Valeryl-L-carnitine	0.020	0.142						■	■			■	■
Pantothenic acid	0.023	0.149	■					■	■			■	■
Dimethylglycine Choline	0.023	0.149			■			■	■			■	■
L-Proline	0.028	0.169			■			■	■			■	■
S-Adenosylmethionine	0.030	0.172						■	■			■	■
Oxoglutaric acid	0.032	0.180	■					■	■			■	■
2-Aminooctanoic acid	0.036	0.184			■			■	■			■	■
Uridine	0.036	0.184						■	■			■	■

^a One-way analysis of variance (ANOVA), if significant (FDR-adjusted p value < 0.2), followed by Fisher's LSD post-hoc analysis. The significant pairwise Fisher's LSD post-hoc tests at a 5% level are indicated with filled black boxes. Groups 1, 2, 3, 4 and 5 represent plasma samples collected at pre-treatment, 1.5, 5.5, 28, and 48 h following the start of irinotecan infusion.

Supplementary Table 3 Significantly changed metabolites following 1.5-h intravenous infusion of irinotecan in combination with veliparib (on Cycle 2 Day 8)

Name	p-value	FDR	Pairwise Fisher's LSD post-hoc test											
			1-2	1-3	1-4	1-5	2-3	2-4	2-5	3-4	3-5	4-5		
N- α -acetyllysine	1.89E-08	2.46E-06	■											
Thymine	8.45E-08	5.49E-06	■											
Asymmetric dimethylarginine	5.23E-05	0.002		■										
Pantothenic acid	2.12E-04	0.005												
D-Tryptophan	2.05E-04	0.005												
Xanthine	2.01E-04	0.005												
Cystathionine	8.09E-04	0.015												
N-Acetylglutamic acid	9.91E-04	0.016												
Phenylalanine	0.001	0.020												
Aminoadipic acid	0.002	0.023												
Ethanolamine	0.002	0.023												
L-Proline	0.003	0.036												
Propionyl-L-carnitine	0.005	0.048												
5-Hydroxyindoleacetic-acid	0.006	0.054												
Guanosine	0.007	0.054												
Malonyl-L-carnitine	0.007	0.054												
Shikimic acid	0.007	0.054												
L-Acetylcarnitine	0.008	0.055												
L-Malic acid	0.012	0.080												
Creatinine	0.013	0.082												
Oxaloacetate	0.013	0.082												
Hypoxanthine	0.015	0.085												
Carnitine	0.015	0.085												
Inosine	0.024	0.128												
Valeryl-L-carnitine	0.026	0.133												
N-Acetyl-L-alanine	0.027	0.133												
Dimethylglycine Choline	0.028	0.133												
Threonine	0.031	0.146												
Imidazoleacetic acid	0.037	0.160												
Sorbitol	0.037	0.160												
Arginine	0.039	0.165												
L-Alanine	0.043	0.173												
Sarcosine	0.047	0.183												

^a One-way analysis of variance (ANOVA), if significant (FDR-adjusted p value < 0.2), followed by Fisher's LSD post-hoc analysis. The significant pairwise Fisher's LSD post-hoc tests at a 5% level are indicated with filled black boxes. Groups 1, 2, 3, 4 and 5 represent plasma samples collected at pre-treatment, 1.5, 5.5, 28, and 48 h following the start of irinotecan infusion.