

Table SI. Comparison of metabolite changes ( $\Delta$ ) between baseline (fraction 0) and end of radiotherapy (fraction 38) between AE(+) and AE(-) groups, with and without exclusion of the UDCA-treated patient (patient 7).

Metabolite	AE(+) (n=7) versus AE(-) (n=4)			AE(+) (n=6) versus AE(-) (n=4) (excluding the UDCA-treated patient)		
	AE(+) $\Delta$ [median (range); $\mu\text{M}$ ]	AE(-) $\Delta$ [median (range); $\mu\text{M}$ ]	P-value	AE(+) $\Delta$ [median (range); $\mu\text{M}$ ]	AE(-) $\Delta$ [median (range); $\mu\text{M}$ ]	P-value
CE (20:4)	0.001 (-0.030 to 0.073)	-0.0230 (-0.0610 to 0.0250)	0.2303	0.0075 (-0.0300 to 0.0730)	-0.0230 (-0.0610 to 0.0250)	0.2571
TDCA	0.001 (-0.030 to 0.073)	-0.0055 (-0.006 to -0.0010)	0.5714	0.0030 (-0.0080 to 0.0110)	-0.0055 (-0.0060 to -0.0010)	0.3697
TG (18:0_32:2)	0.001 (-0.007 to 0.004)	-0.0025 (-0.0180 to 0.0130)	0.8285	0.0010 (-0.0070 to 0.0040)	-0.0025 (-0.0180 to 0.0130)	0.7545
TG (18:3_34:1)	0.0001 (-0.008 to 0.007)	0.0035 (0.000 to 0.0160)	0.3809	0.0010 (-0.0020 to 0.0070)	0.0035 (0.0000 to 0.0160)	0.2485
PC aa C42:2	-0.001 (-0.021 to 0.010)	0.0105 (0.0040 to 0.0130)	0.0666	-0.0015 (-0.0210 to 0.0100)	0.0105 (0.0040 to 0.0130)	0.0667
TG (16:0_38:1)	-0.015 (-0.0300 to 0.0100)	0.0185 (0.0100 to 0.0250)	0.0190	-0.0055 (-0.0300 to 0.0100)	0.0185 (0.0100 to 0.0250)	0.0121
PC ae C42:1	-0.004 (-0.016 to 0.007)	-0.012 (-0.104 to 0.037)	0.4476	-0.0040 (-0.0160 to 0.0070)	0.0025 (-0.0130 to 0.0040)	0.4363
FA (20:2)	-0.012 (-0.104 to 0.037)	0.019 (-0.010 to 0.096)	0.1142	-0.0180 (-0.0100 to 0.0960)	0.0190 (-0.0100 to 0.0960)	0.1636
DG (18:1_18:1)	-0.013 (-0.027 to 0.009)	0.0245 (-0.017 to 0.038)	0.0066	-0.0185 (-0.0270 to 0.0090)	0.0245 (-0.0170 to 0.0380)	0.0727

Changes in metabolite levels ( $\Delta$ ) were calculated for each patient as the difference between metabolite levels at the end of radiotherapy (fraction 38) and baseline (fraction 0). These  $\Delta$  values were compared between the AE(+) and AE(-) groups using the Mann-Whitney U test. Only nominal P-values are shown. Sensitivity analysis was performed by excluding the UDCA-treated patient (patient no. 7). AE, adverse event; DG, diglyceride; FA, fatty acid; PC, phosphatidylcholine; TDCA, taurodeoxycholic acid; TG, triglyceride; UDCA, ursodeoxycholic acid.

Table SII. Correlation-based sensitivity analysis of patient-level Spearman's rank correlation coefficients ( $\rho$ ) with and without exclusion of the UDCA-treated patient (patient 7).

Metabolite	AE(+) (n=7) versus AE(-) (n=4)		AE(+) (n=6) versus AE(-) (n=4) (excluding the UDCA-treated patient)	
	P-value	Q-value	P-value	Q-value
CE (20:4)	0.07	0.81	0.07	0.79
TDCA	0.01	0.49	0.01	0.64
TG (18:0_32:2)	0.02	0.65	0.02	0.74
TG (18:3_34:1)	0.01	0.49	0.01	0.64
PC aa C42:2	0.01	0.49	0.01	0.64
TG (16:0_38:1)	0.01	0.49	0.01	0.64
PC ae C42:1	0.01	0.51	0.02	0.64
FA (20:2)	0.05	0.81	0.04	0.80
DG (18:1_18:1)	0.23	0.93	0.26	0.95

Correlation-based comparisons were performed using patient-level Spearman's rank correlation coefficients ( $\rho$ ). Group differences in  $\rho$  were assessed using the Mann-Whitney U test. P-values were adjusted for multiple testing using the Benjamini-Hochberg false discovery rate procedure. Sensitivity analysis was performed by excluding the UDCA-treated patient (patient no. 7). AE, adverse event; DG, diglyceride; FA, fatty acid; PC, phosphatidylcholine; TDCA, taurodeoxycholic acid; TG, triglyceride; UDCA, ursodeoxycholic acid.

Table SIII. Enzymes and genes associated with the phosphatidylcholine-fatty acid interaction network identified by OmicsNet analysis.

<b>A. Triglyceride-associated enzymes and genes</b>		
<b>Gene/enzyme</b>	<b>Name</b>	<b>KEGG KO</b>
LIPF	Gastric triacylglycerol lipase	K14452
PNLIPRP1	Pancreatic lipase-related protein 1	K14074
PNLIPRP2	Pancreatic lipase-related protein 2	K14075
PNLIPRP3	Pancreatic lipase-related protein 3	K14076
PNLIP	Pancreatic triacylglycerol lipase	K14073
AADAC	Arylacetamide deacetylase	K13616
PNPLA2	Patatin-like phospholipase domain-containing protein 2	K16816
PNPLA3	Patatin-like phospholipase domain-containing protein 3	K13534
DGAT1	Diacylglycerol O-acyltransferase 1	K11155
DGAT2	Diacylglycerol O-acyltransferase 2	K11156
LIPE	Hormone-sensitive lipase	K07188
LPL	Lipoprotein lipase	K01059
LIPG	Endothelial lipase	K22284
LIPC	Hepatic triacylglycerol lipase	K22283
MOGAT3	2-acylglycerol O-acyltransferase 3	K14456
<b>B. Cholesterol ester-associated enzymes and genes</b>		
<b>Gene/enzyme</b>	<b>Name</b>	<b>KEGG ID</b>
SOAT1	Sterol O-acyltransferase 1	K00637
SOAT2	Sterol O-acyltransferase 2	K00637

LIPA

Lysosomal acid lipase/cholesteryl ester hydrolase

K01052

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**C. Triacylglycerol-cholesteryl ester interaction enzymes and genes**

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**Gene/enzyme**

**Name**

**KEGG ID**

CEL

Bile salt-activated lipase

K12298

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CE, cholesteryl ester; KEGG, Kyoto Encyclopedia of Genes and Genomes; KO, KEGG Orthology.

Table SIV. Enzymes and genes associated with the fatty acid-diglyceride/triglyceride interaction network identified by OmicsNet analysis.

<b>Gene/enzyme</b>	<b>Name</b>	<b>KEGG KO</b>
PLA2G2E	Phospholipase A2 group IIE	K01047
PLA2G16	HRAS-like suppressor 3	K16817
PLB1	Phospholipase B1	K14621
PLA2G4B	Cytosolic phospholipase A2 $\beta$	K16342
PLA2G4D	Cytosolic phospholipase A3 $\delta$	K16342
PLA2G2F	Phospholipase A2 group IIF	K01047
PLA2G6	85/88 kDa calcium-independent phospholipase A2	K16343
PLA2G3	Phospholipase A2 group3	K01047
CLC	Eosinophil lysophospholipase	K13334
PNPLA7	Patatin-like phospholipase domain-containing protein 7	K14676
PLA2G12A	Phospholipase A2 group XIIA	K01047
PLAAT2	Phospholipase A and acyltransferase 2	K16817
LYPLA1	Acyl-protein thioesterase 1	K06128
PLA2G4A	Cytosolic phospholipase A2	K16342
LYPLA2	Acyl-protein thioesterase 2	K06130
PLA2G10	Phospholipase A2 group 10	K01047
ASPG	60 kDa lysophospholipase	K13278
PLA2G4C	Cytosolic phospholipase A2 $\gamma$	K16342
PLA2G4F	Cytosolic phospholipase A2 $\zeta$	K16342
PLA2G2C	Phospholipase A2 putative inactive group IIC	K01047
PLA2G15	Phospholipase A2 group XV	K06129
PNPLA6	Neuropathy target esterase	K14676

PLA2G2A	Phospholipase A2	K01047
(JMJD7-)-PLA2G4B	Cytosolic phospholipase A2 $\beta$	K16342
PLA2G2D	Phospholipase A2 group IID	K01047
PLA2G1B	Phospholipase A2	K01047
PLA2G5	Phospholipase A2 group V	K01047
PLA2G12B	Phospholipase A2-like protein group XIIB	K01047

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Multiple genes may share the same KEGG KO identifier because KO represents a functional orthology group. FA, fatty acid; KEGG, Kyoto Encyclopedia of Genes and Genomes; KO, KEGG Orthology; PC, phosphatidylcholine.

Table SV. Enzymes associated with the hypothesized triglyceride-fatty acid lipolysis pathway identified in the network analysis.

<b>Gene/enzyme</b>	<b>Name</b>	<b>KEGG KO</b>
LIPH	Lipase member H	K19404
PNPLA2	Patatin-like phospholipase domain-containing protein 2	K16816
PNLIPRP3	Pancreatic lipase-related protein 3	K14076
LIPG	Endothelial lipase	K22284
AADAC	Arylacetamide deacetylase	K13616
CEL	Bile salt-activated lipase	K12298
LIPC	Hepatic triacylglycerol lipase	K22283
PNLIPRP2	Pancreatic lipase-related protein 2	K14075
PNPLA3	Patatin-like phospholipase domain-containing protein 3	K13534
PNLIP	Pancreatic triacylglycerol lipase	K14073
PNLIPRP1	Inactive pancreatic lipase-related protein 1	K14074

KEGG, Kyoto Encyclopedia of Genes and Genomes; KO, KEGG Orthology.