

**Table S1. Metabolites Associated with Psychoneurological Symptoms Pre- Chemotherapy Cycle (T1)**

Variable	Metabolic pathways	Overlap size	Pathway size	<i>p-value</i>	Metabolites
Pain	Fatty acid activation	7	51	.005	Linoleic acid (all cis C18:2) n-6; Octadecadienoate (n-C18:2);(9E)-Octadecenoic acid; Hexadecanoate (n-C16: 0); Octadecenoate; Octadecatrienoic acid; all-cis-tetracosapentaenoate
	Fatty acid metabolism	5	29	.005	Octadecenoate (n-C18:1); Dimethylnonanoyl carnitine; Linoleic acid (all cis C18:2) n-6; Hexadecanoate (n-C16: 0); Octadecadienoate (n-C18:2) n-6
	De novo fatty acid biosynthesis	5	35	.013	E857; Octadecatrienoic acid; (9E)-Octadecenoic acid; Linoleic acid all cis C18:2); Hexadecanoate (n-C16: 0)
	Purine metabolism	5	36	.014	N1-(5-Phospho-D-ribose) glycinamide; dATP; Deoxyuridine; Guanosine; 5-Amino-4-imidazolecarboxamide
	Xenobiotics metabolism	5	45	.037	Naphthalene; 1,2-Dihydronaphthalene-1,2-diol; Hexadecanoate (n-C16: 0); E500; 4-Nitrophenyl sulfate
Fatigue	Linoleate metabolism	4	46	.046	E271; (9Z, 11E)- (13S)-13-Hydroperoxyoctadeca-9, 11-dienoic acid; E661; Lysophosphatidylcholine
Anxiety	Tryptophan metabolism	7	71	.034	Indole-3-acetaldehyde; 4-Hydroxy-2-quinolinecarboxylic acid; Indole-3-acetate; Xanthurenic acid; alpha-N-Phenylacetyl-L-glutamine; Formyl-5-hydroxykynurenamine; 5-Hydroxyindoleacetate
	Valine, leucine and isoleucine degradation	3	15	.017	3-methyl-2-oxobutanoate; Guanidinoacetate; L-leucine
Depressive symptoms	3-oxo-10R-octadecatrienoate beta-oxidation	4	16	.015	3-oxo-10(R)-hydroxy-octadeca-6E,8E,12Z-trienoate; 3(S),6(R)-dihydroxy-tetradec-8Z-enoate; 3-oxo-6(R)-hydroxy-tetradec-8-cis-enoate; 6(S)-hydroxy-tetradeca-2E,8Z-

	Linoleate metabolism	7	46	.028	dienoate (9Z,11E)-13-Hydroperoxyoctadeca-9,11-dienoic acid; E661; E902; 9.10-hydroxyoctadec-12(Z)-enoate;
	Tryptophan metabolism	9	71	.044	Lysophosphatidylcholine; E730; E271 Xanthurenic acid; Indole-3-acetaldehyde; Nicotinate; E370; 4-hydroxy-2-quinolinecarboxylic acid; Indole-3-acetate; 5-Methoxyindoleacetate; Formyl-5-hydroxykynurenamine; 5-Hydroxyindoleacetate
Ordinal PNS cluster	Tryptophan metabolism	9	71	.002	Indole-3-acetate; Alpha-N-phenylacetyl-L-glutamine; 4-Hydroxy-2-quinolinecarboxylic acid; N-Acetylserotonin; Xanthurenic acid; Nicotinate; Serotonin; E680; Formyl-5-hydroxykynurenamine

T1, pre-chemotherapy; PNS, psychoneurological symptoms

Overlap size means significant metabolite hits associated with the outcomes; metabolic pathways with an overlap size < 3 were removed from our findings. Pathway size means total number of KEGG metabolites in the pathways. Metabolites represent some examples of identified metabolites that are associated with outcome variables (PNS and the PNS cluster).

**Table S2. Metabolites Associated with Psychoneurological Symptoms Post-Chemotherapy Cycle (T2)**

Variable	Metabolic pathways	Overlap size	Pathway size	<i>p-value</i>	Metabolites
Pain	Glycerophospholipid metabolism	12	60	< .001	(6Z,9Z,12Z)- Octadecatrienoic acid; Choline Phosphate; D-Galactose; Lysophosphatidylcholine; D-serine; Choline phosphate; Hydroxyeicosatetraenoate; Phosphatidylcholine; Acetylcholine; sn-Glycero-3-phosphocholine; 1-Alkyl-2-lyso-sn-glycero-3-phosphocholine; Dehydrosphinganine
	Glycosphingolipid metabolism	6	28	.002	Choline phosphate; D-Galactose; Hexadecanoate(n0C16: 0); E608; D-Serine; 3-Dehydrosphinganine
	Fatty Acid Metabolism	5	29	.010	Ocdcy, octadecadienoate (n-C18:2); Octadecanoate (n-C16: 0); Octadecanoate (n-C18: 0); Hexadecanoate(n-C16: 0); Dodecanoate (n-C12: 0)
	De novo fatty acid biosynthesis	5	35	.022	(6Z,9Z,12Z)- Octadecatrienoic acid; Octadecanoate(n-C18: 0); Octadecanoate(n-C18: 0); Hexadecanoate(n-C16: 0); Dodecanoate(n-C12: 0)
	Vitamin B3 (nicotinate and nicotinamide) metabolism	3	20	.049	N1-Methyl-4-pyridone-5-carboxamide; 1mncam, 1-Methylnicotinamide; Nicotinate
Fatigue	Xenobiotics metabolism	7	45	.003	Dodecanoate (n-C12: 0); 1,2-Dihydronaphthalene-1,2-diol; E948; E219; 4-Nitrophenyl sulfate; 1-Nitronaphthalene; 1-Ntro-5,6-dihydroxy-dihydronaphthalene
	Vitamin B6 (pyridoxine) metabolism	3	10	.005	Pyridoxamine; E343; 4-Pyridoxate
	Tryptophan metabolism	8	71	.012	Formyl-5-hydroxykynurenamine; 5-Hydroxyindoleacetate; Nicotinate; N-Methyltryptamine; E356; D-Galactose; Tetrahydrobiopterin-4a-carbinolamine; 1-Ntro-5,6-dihydroxy-dihydronaphthalene

	Drug metabolism - cytochrome P450	3	22	.045	5-Hydroxyindoleacetate; Didemethylcitalopram; E423
Anxiety	Tryptophan metabolism	11	71	.013	Nicotinate; 1,2-dehydrosalsolinol; 5-Hydroxy-L-tryptophan; Formylkynurenine; Formyl-5-hydroxykynurenamine; 5-Hydroxyindoleacetate; N-Methylserotonin; Indolepyruvate; E806; 1-Nitro-5,6-dihydroxy-dihydronaphthalene; N-Acetylserotonin
	Drug metabolism - cytochrome P450	5	22	.015	Didemethylcitalopram; 5-hydroxyindoleacetate; 3-Carbamoyl-2-phenylpropionaldehyde; p-Hydroxyfelbamate; E423
	Glycerophospholipid metabolism	9	60	.026	Choline phosphate; D-Serine; Tetrahydropteridine; sn-Glycero-3-phosphocholine; Arachidonic acid; sn-Glycero-3-phosphoethanolamine; Glycerol 3-phosphate; sn-glycero-3-Phospho-1-inositol; Diacylglycerol
	Urea cycle/amino group metabolism	9	62	.031	O-methylhippurate; E132; (2R,4S)-2,4-Diaminopentanoate; L-Arginine; E673; N-Acetyl-L-glutamine; Agmatine; N-Methylphenylethanolamine; L-Proline
	Glycine, serine, alanine and threonine metabolism	8	54	.035	2-Aminoacrylate; (2R,4S)-2,4-Diaminopentanoate; Betaine aldehyde; D-Serine; L-Arginine; E673; L-Threonine; E806
	Glycosphingolipid metabolism	5	28	.037	N-Acetyl-D-galactosamine; Hexadecenal; D-Serine; Choline phosphate; Psychosine
	Vitamin B3 (nicotinate and nicotinamide) metabolism	4	20	.038	L-Arginine; E806; Nicotinate; E673
Depressive symptoms	Alanine and aspartate metabolism	4	14	.010	L-Glutamate; E806; L-Arginine; L-Aspartate
	Glycerophospholipid metabolism	10	60	.009	Tetrahydropteridine; D-Serine; 1-Alkyl-2-lyso-sn-glycero-3-phosphocholine; Phosphatidic acid; sn-Glycero-3-

	3-oxo-10R-octadecatrienoate beta-oxidation	4	16	.016	phosphocholine; sn-glycero-3-phospho-1- inositol; Lysophosphatidylcholine; Choline phosphate; Sterol; Diacylglycerol 3(S),6(R)-dihydroxy-tetradec-8Z-enoate; 3(S),8(R)-dihydroxy-6E,10Z- hexadecadienoate; 8(S)-hydroxy-hexadeca- 2E,4E,6E,10Z-tetraenoate; 3(S),6(R)- dihydroxy-tetradec-8Z-enoate
	Glycine, serine, alanine and threonine metabolism	8	54	0.029	Betaine aldehyde; (2R,4S)-2,4- Diaminopentanoate; D-Serine; 2- Aminoacrylate; L-Glutamate; Isobutyrylglycine; L-Arginine; E806
	Selenoamino acid metabolism	3	12	0.031	E806; D-Serine; Deoxyguanosine
	Methionine and cysteine metabolism	7	50	0.048	L-Glutamate; D-Serine; Thiosulfate; 2- Aminoacrylate; E883; E806; Deoxyguanosine
	Vitamin B3 (nicotinate and nicotinamide) metabolism	4	20	.033	L-Glutamate; E806; L-Arginine; L- Aspartate
Ordinal PNS cluster	Fatty acid metabolism	5	29	.014	Hexadecenoate(n-C16:1); Octadecenoate(n- C18:1); Hexadecenoate(n-C16:0); Dodecanoate(n-C12: 0); Octadecadienoate(n-C18:2)
	Fatty acid activation	6	51	.045	Octadecenoate(n-C18:1); (6Z,9Z,12Z)- Octadecatrienoic acid; Hexadecenoate(n- C16:0); Butanoic acid; Octadecadienoate(n- C18:2); Hexadecenoate(n-C16:1)
	Glycosphingolipid metabolism	4	28	.044	Ethanolamine phosphate; N-Acetyl-D- galactosamine; Hexadecenoate(n-C16:0); D-Serine
	3-oxo-10R-octadecatrienoate beta-oxidation	4	16	.006	8(S)-hydroxy-hexadeca-4E,6E-10Z- trienoate; 8(S)-hydroxy-hexadeca- 2E,4E,6E,10Z-tetraenoate; 3(S),6(R)- dihydroxy-tetradec-8Z-enoate; E52
	Tryptophan metabolism	8	71	.033	4-(2-Amino-3-hydroxyphenyl)-2,4- dioxobutanoate; Tetrahydrobiopterin-4a- carbinolamine; N-Methyltryptamine; E356;

5-Hydroxy-L-tryptophan; 1-Nitro-5,6-dihydroxy-dihydronaphthalene; 5-Hydroxyindoleacetate; Formyl-5-hydroxykynurenamine

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