

**THE METABOLOMIC SIGNATURE OF OPA1 DEFICIENCY  
IN RAT PRIMARY CORTICAL NEURONS SHOWS ASPARTATE/GLUTAMATE  
DEPLETION AND PHOSPHOLIPIDS REMODELING**

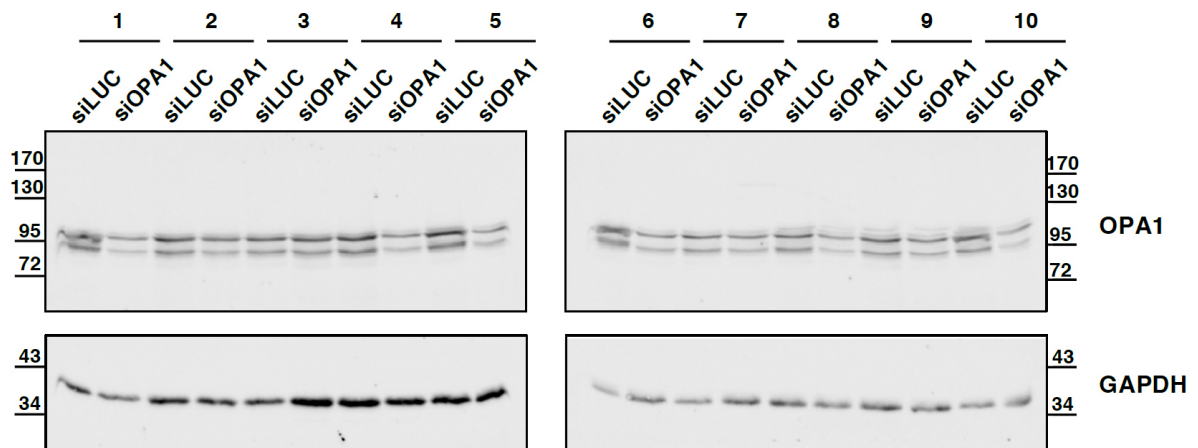
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Biochemical family		Number of metabolites	Method used for quantitation	
Carnitine (C0) and acyl-carnitines (AC)		40	FIA-MS/MS	
Amino acid (AA)		21	LC-MS/MS	
Biogenic amine (BA)		21	LC-MS/MS	
Hexose (H1)		1	FIA-MS/MS	
Lipids	Lysophosphatidylcholine (lyso PC)	14	FIA-MS/MS	
	Phosphatidylcholine (PC)	Diacyl-PC (PC aa)	38	FIA-MS/MS
		Alkyl-acyl-PC (PC ae)	38	FIA-MS/MS
	Sphingomyelins (SM)	15	FIA-MS/MS	

**Supplementary Table 1.** Biochemical families of metabolites quantified in Biocrates® Absolute IDQ p180 kit. FIA-MS/MS: Flow Injection Analysis-Tandem mass spectrometry. LC-MS/MS: Liquid Chromatography-Tandem mass spectrometry.

<b>Ratio or sum</b>	<b>Metabolic significance</b>
<b>Ratio of asymmetrically demethylated arginine to total unmodified arginine (ADMA/Arg)</b>	Inhibition of nitric oxide synthase (NOS)
<b>Ratio of total demethylated arginine to total unmodified arginine (Total DMA/Arg)</b>	Activity of protein arginine methyl transferase
<b>Ratio of citrulline to arginine (Cit/Arg)</b>	Activity of NOS
<b>Ratio of citrulline to ornithine (Cit/Orn)</b>	Activity of ornithine carbamoylphosphate transferase
<b>Ratio of ornithine to arginine (Orn/Arg)</b>	Activity of arginase
<b>Ratio of tyrosine to phenylalanine (Tyr/Phe)</b>	Activity of phenylalanine hydroxylase
<b>Ratio of sulfoxidized methionine to total unmodified methionine (Met-SO/Met)</b>	Measure of systemic oxidative stress
<b>Ratio of kynurenine to tryptophan (Kyn/Trp)</b>	Rate of tryptophan degradation to niacin (immunosuppression/tolerance)
<b>Ratio of serotonin to tryptophan (Serotonin/Trp)</b>	Rate of tryptophan degradation to serotonin
<b>Ratio of putrescine to ornithine (Putrescine/Orn)</b>	Activity of ornithine decarboxylase
<b>Ratio of spermidine to putrescine (Putrescine/Spermidine)</b>	Activity of spermidine synthase
<b>Ratio of spermine to spermidine (Spermine/Spermidine)</b>	Activity of spermine synthase
<b>Ratio of acetylcarnitine to free carnitine (C2/C0)</b>	Measure of $\beta$ -oxidation of even numbered fatty acids (FA)
<b>Ratio of short chain acylcarnitines to free carnitine ((C2+C3)/C0)</b>	Measure of overall $\beta$ -oxidation activity
<b>Ratio of long chain acylcarnitines to free carnitine ((C16+C18)/C0)</b>	Activity of carnitine palmitoyltransferase I
<b>Ratio of dicarboxy-acylcarnitines to total acylcarnitines (Total AC-DC/Total AC)</b>	Indicator of $\omega$ -oxidation of FA.
<b>Sum of saturated FA in diacyl PC (SFA aa)</b>	Indicator of lipid composition on SFA aa
<b>Sum of saturated FA in acyl-alkyl PC (SFA ae)</b>	Indicator of lipid composition on SFA ae
<b>Sum of mono-unsaturated FA in diacyl PC (MUFA aa)</b>	Indicator of lipid composition on MUFA aa
<b>Sum of mono-unsaturated FA in acyl-alkyl PC (MUFA ae)</b>	Indicator of lipid composition on MUFA ae
<b>Sum of poly-unsaturated FA in diacyl PC (PUFA aa)</b>	Indicator of lipid composition on PUFA aa
<b>Sum of poly-unsaturated FA in acyl-alkyl (PUFA ae)</b>	Indicator of lipid composition on PUFA ae
<b>Unsaturated (MUFA+ PUFA) to saturated FA in diacyl PC (UFA/SFA aa)</b>	Measure of the activity of desaturases on diacyl PC
<b>Unsaturated (MUFA+ PUFA) to saturated FA in acyl-alkyl PC (UFA/SFA ae)</b>	Measure of the activity of desaturases on acyl-alkyl PC
<b>Ratio of lysoglycerophosphocholines to glycerophosphocholines (Total lysoPC/ Total PC)</b>	Indicator of phospholipase activity

**Supplementary Table S2.** Ratios or sums of metabolites selected for their potential metabolic significance in the setting of cultured cells.



**Supplementary Fig. S3:** OPA1 (higher panel) and GAPDH (lower panel) cropped immunoblots showing at DIV9 the quantities of proteins in neurons transfected with siLUC or siOPA1 in 10 independent experiments. The two 9% polyacrylamid gels required for this analysis were processed in parallel and membranes were exposed with the same duration. The full length immunoblot is showed below.

