

Comparative NMR metabolomics of the responses of A2780 human ovarian cancer cells to clinically established Pt-based drugs

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Electronic Supplementary Information (ESI)

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Table S1. List of assigned and quantified metabolites in cell lysates (endo-) and growing media (exo-) with the respective HMDB code and the ¹H NMR resonance assignment; s= singlet; d= doublet; t=triplet; dd= doublet of doublets; ddd= doublet of doublets of doublets; dt= doublet of triplets; m= multiplet.

Metabolites	Endo-	Exo-	HMDB ID	NMR assignment
4-Hydroxy-L-proline	x	x	HMDB0000725	2.14 (m); 2.42 (m); 3.36 (m); 3.46 (ddd); 4.33 (dd); 4.67 (m)
Acetate	x	x	HMDB0000042	1.93 (s)
Adenosine-X-phosphate	x		HMDB0000045 HMDB0001341 HMDB0000538	8.61 (s)
L-Aspartate		x	HMDB0000191	2.67 (m); 2.83 (m); 3.87 (m)
Choline	x		HMDB0000097	3.19 (s); 3.51 (dd); 4.06 (m)
Citrate		x	HMDB0000094	2.66 (d); 2.52 (d)
Creatine	x		HMDB0000064	3.02 (s); 3.92 (s)
D-Glucose	x	x	HMDB0000122	3.23 (dd); 3.40 (m); 3.46 (m); 3.52 (dd); 3.73 (m); 3.82 (m); 3.89 (dd); 4.63 (d)
Ethanol	x	x	HMDB0000108	1.17 (t); 3.65 (q)
Formate	x	x	HMDB0000142	8.45 (s)
Fumarate	x	x	HMDB0000134	6.51 (s)
Glutathione	x		HMDB0000125	2.16 (m); 2.54 (m); 2.97 (dd); 3.78 (m); 4.20 (q)
Glycerophosphocholine	x		HMDB0000086	3.20 (s); 3.64 (m) 3.90 (m); 4.30 (m)
Glycine	x	x	HMDB0000123	3.54 (s)
Guanosine-X-phosphate	x		HMDB0001397 HMDB0001201 HMDB0001273	5.93 (d)
Lactate	x	x	HMDB0000190	1.32 (d); 4.10 (q)
L-Alanine	x	x	HMDB0000161	1.47 (d); 3.77 (q)
L-Arginine		x	HMDB0000517	1.68 (m); 1.90 (m); 3.23 (t); 3.76 (t)
L-Asparagine	x	x	HMDB0000168	2.67 (m); 2.83 (m); 3.87 (dd)
L-Cystine		x	HMDB0000192	3.18 (dd); 3.37 (dd); 4.10 (dd)
L-Glutamate	x	x	HMDB0000148	2.04 (m); 2.12 (m); 2.34 (m); 3.75 (dd)
L-Glutamine	x	x	HMDB0000641	2.12 (m); 2.45 (m); 3.77 (t)

L-Histidine		x	HMDB0000177	3.16 (dd); 3.23 (dd); 3.98 (dd); 7.09 (d); 7.9 (d)
L-Isoleucine	x	x	HMDB0000172	0.93 (t); 1.00 (d); 1.25 (m); 1.46 (m); 1.97 (m); 3.66 (d)
L-Leucine	x	x	HMDB0000687	0.95 (t); 1.70 (m); 3.72 (m)
L-Lysine	x	x	HMDB0000182	1.46 (m); 1.71 (m); 1.89 (m); 3.02 (t); 3.74 (t)
L-Methionine		x	HMDB0000696	2.16 (m); 2.63 (t); 3.85 (dd)
L-Ornithine		x	HMDB0000214	1.80 (m); 1.93 (m); 3.04 (m); 3.77 (m)
L-Phenylalanine		x	HMDB0000159	3.11 (m); 3.27 (m); 3.98 (m); 7.37 (m)
L-Proline	x	x	HMDB0000162	2.00 (m); 2.08 (m); 2.34 (m); 3.32 (dt); 3.41 (m); 4.12 (dd)
L-Serine		x	HMDB0000187	3.83 (dd); 3.96 (m)
L-Tyrosine	x	x	HMDB0000158	3.02 (dd); 3.17 (dd); 3.92; (dd); 6.88 (m); 7.17 (m)
L-Valine	x	x	HMDB0000883	0.98 (d); 1.03 (d); 2.26 (m); 3.60 (d)
Methanol	x		HMDB0001875	3.34 (s)
Myo-inositol	x	x	HMDB0000211	3.27 (t); 3.54 (dd); 3.61 (t); 4.05 (t)
Niacinamide	x		HMDB0001406	7.58 (dd); 8.23 (dd); 8.70 (dd); 8.92 (s)
Phosphocholine	x		HMDB0001565	3.21 (s); 3.59 (m); 4.19 (m)
Phosphocreatine	x		HMDB0001511	3.03 (s); 3.94 (s)
Pyroglutamate		x	HMDB0000267	2.02 (m); 2.39 (m); 2.50 (m); 4.17 (dd)
Pyruvate		x	HMDB0000243	2.37 (s)
Succinate	x		HMDB0000254	2.41 (s)
UDP-N-acetyl-galactosamine	x		HMDB0060522	2.04 (s); 3.49 (dt); 3.72 (dd); 3.90 (dd); 4.02 (dd); 4.12 (d); 4.20 (ddd); 4.25 (ddd); 4.37 (dd); 5.63 (dd); 5.97 (d); 7.95 (d)
UDP-N-Acetyl-glucosamine	x		HMDB0000290	2.07 (s); 3.54 (t); 3.80 (m); 3.91 (m); 3.98 (m); 4.17 (m); 4.23 (m); 4.27 (m); 4.35

				(m); 5.50 (dd); 5.96 (m); 7.93 (t); 8.32 (d)
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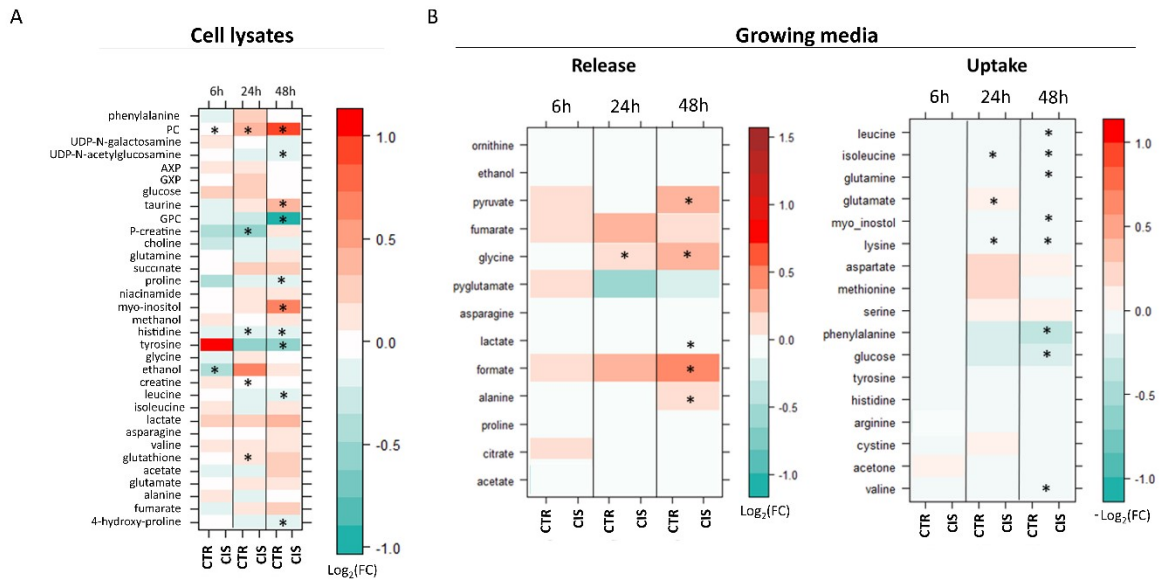


Figure S1. Level plots of Fold Change for cisplatin at 6 h, 24 h and 48 h of treatment; A) Cell lysates: red/green parameters indicate higher/lower concentration in CIS-treated cells with respect to controls samples ($\text{Log}_2(\text{FC})$). B) growth media: red/green parameters indicate higher/lower release ($\text{Log}_2(\text{FC})$) or uptake ($-\text{Log}_2(\text{FC})$), respectively, in CIS-treated cells with respect to controls samples. The brightness of the colors corresponds to the magnitude of the FC. Asterisks indicate statistical significance ($p\text{-value} < 0.05$).

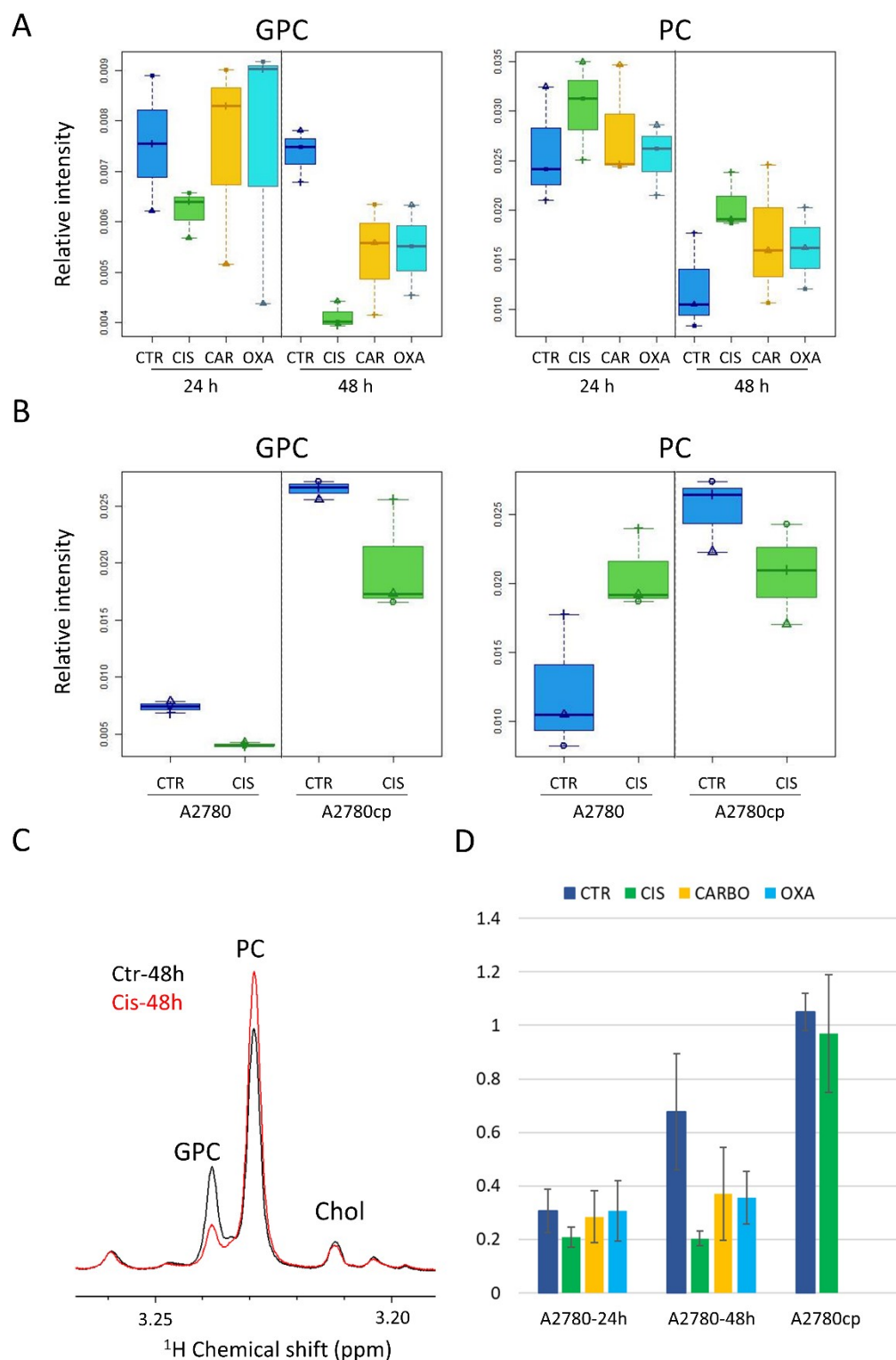


Figure S2. Changes in the levels of glycerophosphocholine (GPC) and phosphocholine (PC) as a function of the different treatments and/or in different cell lines. *A*) Boxplots of the GPC and PC levels at 24 h and 48 h in: control (blue), CIS- (yellow), CARBO- (orange) and OXA-treated (cyan) A2780 cells. *B*) Boxplots of the GPC and PC levels at 48 h in control (blue) and CIS-treated (green) in A2780 and A2780cp cells. *C*) Representative ^1H NMR spectral region containing choline-derivatives signals: control (black trace), CIS-treated (red trace) recorded

for A2780 lysates at 48 h. D) GPC/PC ratio for control (blue bars), CIS- (yellow bars), CARBO- (orange bars) and OXA-treated (cyan bars) A2780 and A2780cp cells. For A2780cp cells, the results of CIS treatment are referred to the condition of equal toxicity.