Electronic supporting material

to

Metallomic study on the metabolism of RAPTA-C and cisplatin in cell culture medium on cell accumulation

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Table S1. ICP-MS settings and operational parameters.

Parameter	Setting
Plasma gas flow rate, L min^{-1}	15
Auxiliary gas flow rate, L min^{-1}	1.0
Sampler	Ni
Skimmer	Ni
Plasma RF power, W	1550
Isotopes registered	^{31}P, ^{57}Fe, ^{59}Co, ^{185}Re, ^{101}Ru, ^{102}Ru, or ^{194}Pt, ^{195}Pt
Data points, s^{-1}	0.926
Nebulizer gas flow rate, L min^{-1}	1.35
Sheath Liquid	20 mM ammonium acetate, 20 ppb Ge, Sc, Re

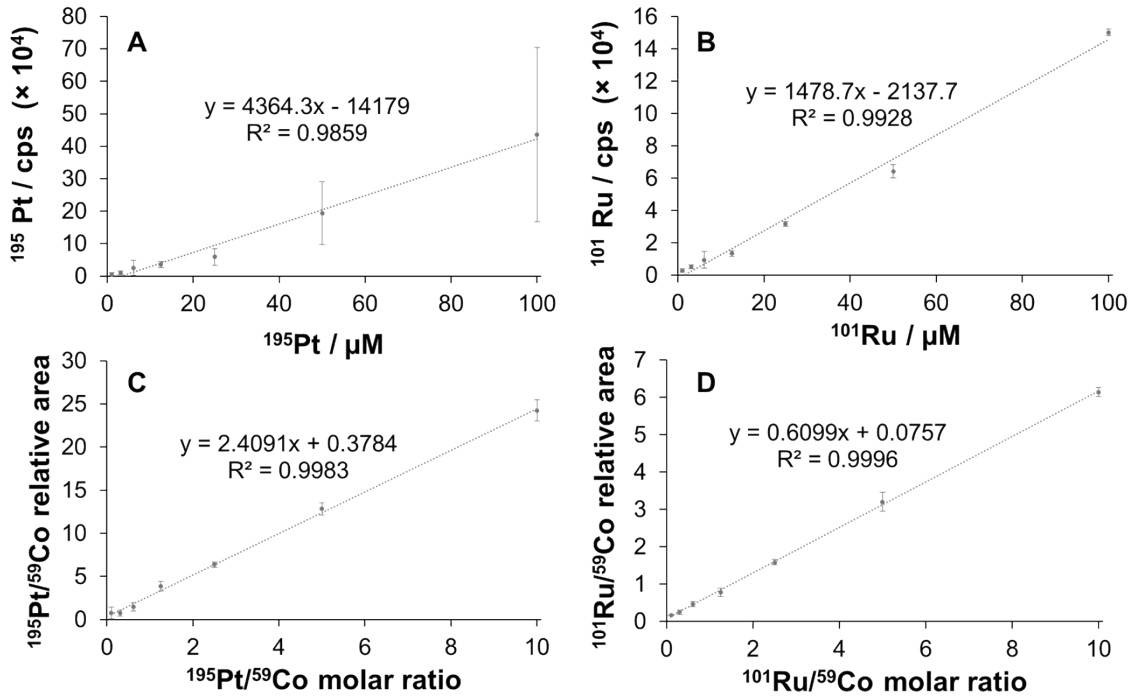

Figure S1. The calibration plots for platinum (A) and ruthenium (B) prepared through cisplatin or RAPTA-C standards of 1.56, 3.06, 6.13, 12.5, 25, 50 and 100 µM, both before (A, B) and after correction with 10 µM of the internal standard [$Co(acac)_3$] (C, D). This resulted in limits of detection (LOD) and limits of quantification (LOQ) for Pt and Ru of 7.6 and 5.5 µM, and 23.3 and 16.5 µM, respectively. Correction with the internal standard [$Co(acac)_3$] lowered the LOD and LOQ to 2.6 and 1.3 µM, and 8.0 and 3.9 µM, respectively.

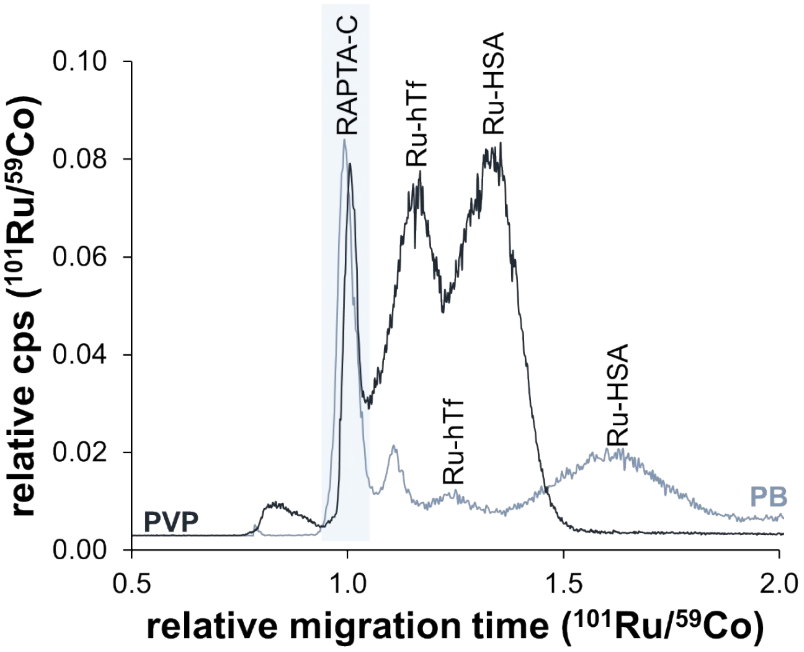

Figure S2. The averaged ^{101}Ru electropherograms of RAPTA-C/HSA/hTf (2:1:1) samples incubated for 96 h at 37 ºC after migration time and peak area correction with the internal standard [Co(acac)$_3$] (10 µM). The data were collected using CE–ICP-MS with capillaries (70 cm, 75 µm ID) coated with either PVP (black) or PB (grey)

Table S2. Comparison of the repeatability of analysis of RAPTA-C/HSA/hTf (2:1:1) samples with PVP- and PB-coated capillaries. Presented are the peak areas and relative standard deviations of the three principal peaks of interest identified in Figure 5 both before and after correction with the internal standard [Co(acac)$_3$] (10 µM), n = 3.

	peak area (± RSD%)			
coating	PVP		PB	
internal standard	– Co / ×10^3 cps	+ Co / a.u.	– Co / ×10^3 cps	+ Co / a.u.
RAPTA-C	100 (± 34%)	1.4 (± 23%)	54 (± 6%)	1.3 (± 7%)
Ru-hTf	340 (± 20%)	4.6 (± 8%)	15 (± 9%)	0.4 (± 6%)
Ru-HSA	500 (± 12%)	6.8 (± 2%)	74 (± 7%)	1.8 (± 2%)

Table S3. The components of the used α-minimum essential medium (MEM),[1] supplemented with 5% fetal calf serum in cell studies.

Components	Molecular weight (g/mol)	mg/L	mM
Amino Acids			
Glycine	75	50	0.67
L-Alanine	89	25	0.28
L-Arginine	211	105	0.50
L-Asparagine-H_2O	132	50	0.38
L-Aspartic acid	133	30	0.23
L-Cysteine hydrochloride-H_2O	176	100	0.57
L-Cystine 2HCl	240	24	0.10
L-Glutamic acid	147	75	0.51
L-Glutamine	146	292	2.00
L-Histidine	155	31	0.20
L-Isoleucine	131	52.4	0.40
L-Leucine	131	52.4	0.40
L-Lysine	146	58	0.40
L-Methionine	149	15	0.10
L-Phenylalanine	165	32	0.19
L-Proline	115	40	0.35
L-Serine	105	25	0.24
L-Threonine	119	48	0.40
L-Tryptophan	204	10	0.049
L-Tyrosine disodium salt	225	52	0.23
L-Valine	117	46	0.39
Vitamins			
Ascorbic acid	176	50	0.28
Biotin	244	0.1	0.00041
Choline chloride	140	1	0.0071
D-Calcium pantothenate	477	1	0.0021
Folic Acid	441	1	0.0023
Niacinamide	122	1	0.0082
Pyridoxal hydrochloride	204	1	0.0049
Riboflavin	376	0.1	0.0003
Thiamine hydrochloride	337	1	0.0030
Vitamin B_{12}	1355	1.36	0.0010
i-Inositol	180	2	0.0111

Table S3. Cont'd.

Components	Molecular weight (g/mol)	mg/L	mM
Inorganic Salts			
Calcium chloride ($CaCl_2$) (anhyd.)	111	200	1.80
Magnesium sulfate ($MgSO_4$) (anhyd.)	120	97.67	0.81
Potassium chloride (KCl)	75	400	5.33
Sodium chloride (NaCl)	58	6800	117.24
Sodium phosphate monobasic (NaH_2PO_4-H_2O)	138	140	1.01
Other Components			
D-Glucose (dextrose)	180	1000	5.56
Lipoic acid	206	0.2	0.0010
Phenol red	376.4	10	0.027
Sodium pyruvate	110	110	1.00

Table S4. The components listed in the certificate of analysis of fetal calf serum by Moregate Biotechnology which was added to α-MEM at 5% (v/v).

Protein content		**Units**
Total protein	36	g L^{-1}
Albumin	57.0	%
Total globulins		
Alpha 1 and Alpha 2	32.9	%
Beta	9.3	%
Gamma	0.8	%
IgG	160.4	mg L^{-1}
Haemoglobin	0.09	mg mL^{-1}
Endotoxin	<1.0000	IU mL^{-1}
Biochemical profile		**Units**
Sodium	136	mmol L^{-1}
Potassium	11.6	mmol L^{-1}
Chloride	99	mmol L^{-1}
Bicarbonate	16	mmol L^{-1}
Anion Gap	21	mmol L^{-1}
Glucose	6.3	mmol L^{-1}
Urea	6.7	mmol L^{-1}
Creatinine	0.228	mmol L^{-1}
Urea/Creatinine ratio	29	
Urate	0.17	mmol L^{-1}
Bilirubin total	9	μmol L^{-1}
Calcium	3.37	mmol L^{-1}
Phosphate	3.17	mmol L^{-1}
Alkaline phosphatase	180	U L^{-1}
Gamma glutamyl transferase	9	U L^{-1}
Alanine transaminase: (glutamic pyruvic transaminse)	10	U L^{-1}
Aspartate transaminase: (glutamic oxaloacetic transaminase)	51	U L^{-1}
Lactate dehydrogenase	691	U L^{-1}
Triglyceride	0.6	mmol L^{-1}
Cholesterol	0.8	mmol L^{-1}

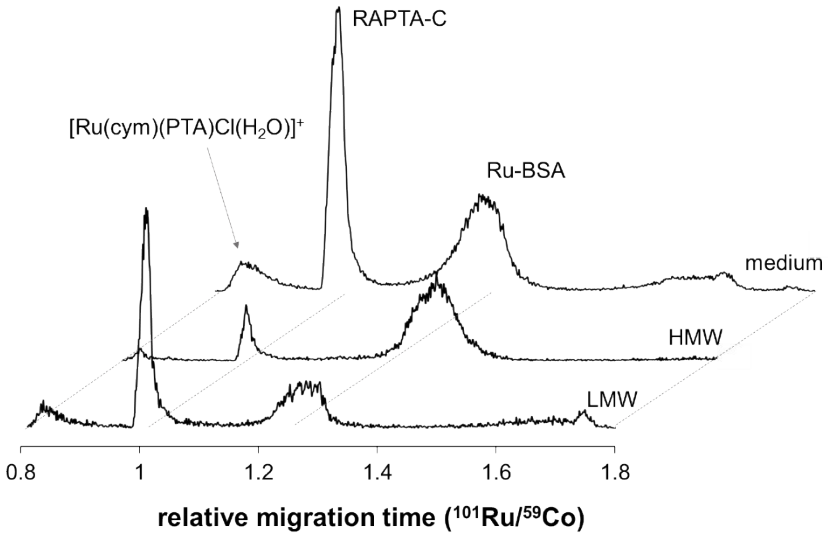

Figure S3. The ^{101}Ru electropherograms of RAPTA-C in cell medium samples after 72 h incubation, and of the HMW and LMW fraction of the same 10 kDa cut-off filtered sample. The samples were analyzed *via* CE–ICP-MS using capillaries (70 cm, 75 μm ID) coated with PVP and the data is shown after migration time and peak area correction with the internal standard [$Co(acac)_3$] (10 μM). Note the presence of an anionic species with a migration time higher that of the Ru-BSA adduct in the LMW fraction.

References

1. T. F. Scientific, *Technical Resources - α-Minimum Essential Medium*, http://www.thermofisher.com/nz/en/home/technical-resources/media-formulation.98.html, Accessed 2017/10/16.