Supporting Information

Methods

Chemicals Cisplatin (*cis*-diamminedichloroplatinum(II), >98%), DMEM-HG (Dulbecco's Modified Eagle Medium high glucose) culture medium, EDTA (ethylenediaminetetraacetic acid, disodium salt dihydrate), penicillin-streptomycin (100x solution), PBS (phosphate buffered saline), sodium hydrogen carbonate, Trypan blue (0.4% solution, prepared in 0.81% sodium chloride and 0.06% dibasic potassium phosphate), and trypsin were purchased from Sigma-Aldrich (UK). FBS (fetal bovine serum) was obtained from Gibco (UK).

Cell Culture The epithelial human breast cancer cell line MDA-MB-231 (human Caucasian triple-negative, claudin-low, breast carcinoma) was purchased from the European Collection of Cell Cultures (ECCAC, Salisbury, UK). These cells lack the oestrogen, progesterone and human epidermal growth factor receptors (ER, PR and HER2), thus being a suitable experimental model of metastasis.

The cells were grown on-site (at the Life Science laboratories of the Research Complex at Harwell), cultured as monolayers, at 37 °C in a humidified atmosphere of 5% CO_2, in DMEM-HG (4500 mg/mL) medium supplemented with 10% (*v/v*) heat inactivated FBS, 1% *(v/v)* penicillin/streptomycin and 0.02 M sodium bicarbonate (pH 7.4). Under these growing conditions, the cell duplication time was found to be 26 h (in accordance with previous reports[1]). Cells were subcultured at *ca.* 80% confluence, using a 1x trypsin-EDTA solution.

Cells were left to grow for 24 h until 60% confluence prior to cisplatin administration (from a 1 mM solution) at 8 (50% cell growth inhibition dosage, IC_{50})[2] and 20 μM concentrations, followed by incubation for 48 h at 37 °C, in a humidified 5% CO_2 atmosphere. The cisplatin solution was prepared in PBS in order to maintain osmolality upon administration to the cells, the drug being readily soluble at the concentrations tested[2].

Optical Vibrational Spectroscopy

***Fourier-transform Infrared Spectroscopy*:** FTIR spectra (in the 400-4000 cm^{-1} range) of lyophilised MDA-MB-231 cells, both untreated and cisplatin-treated, were recorded (at room temperature, in KBr disks *ca.* 0.5% *(w/w)*) in a Bruker Optics Vertex 70 FTIR spectrometer, coupled to a KBr beamsplitter and a liquid nitrogen cooled Mercury Cadmium Telluride (MCT) detector. Each spectrum was the sum of 128 scans, at a 2 cm^{-1} resolution. The error in wavenumbers was estimated to be less than 1 cm^{-1}.

***Raman Spectroscopy*:** Raman spectra (in the 200 – 1800 cm^{-1} and 2750 – 3500 cm^{-1} intervals) of lyophilised MDA-MB-231 cells, both untreated and cisplatin-treated, were recorded in a Horiba Jobin-Yvon T64000 spectrometer in direct configuration mode (focal distance 0.640 m, aperture f/7.5), equipped with a holographic grating of 1800 grooves.mm^{-1}. The entrance slit was set to 200 μm. Rayleigh elastic scattering was rejected by a Notch filter, which reduces its intensity by a factor of 10^6. The detection system was a liquid nitrogen cooled non-intensified 1024×256 pixels (1") CCD. The 514.5 nm line of an Ar^+ laser (Coherent, model Innova 300-05) was used as the excitation radiation, yielding *ca.* 10 mW at the sample position. The spectra were recorded using an Olympus 50× objective (Olympus MSPlan 50XW, NA 0.8, wd 0.47 mm, Japan). A 200 μm confocal pinhole rejected signals from out-of-focus regions of the sample. All spectra were recorded with 15 accumulations and 120 seconds of exposure, at $< 1\ cm^{-1}$ spectral resolution.

All experiments were run at room temperature and the samples were placed onto glass microscope slides.

1. Fiuza SM, Holy J, Batista de Carvalho LAE, Marques MPM (2011) Biologic activity of a dinuclear Pd(II)-spermine complex toward human breast cancer. *Chem Biol Drug Des* 77(6):477-488.
2. Riley CM , Sternson LA (1985) Cisplatin. *Analytical Profiles of Drug Substances*, ed Klaus F (Academic Press), Vol Volume 14, pp 77-105.

Table S1 Main infrared, Raman and INS bands observed for human breast cancer cells (MDA-MB-231).

FTIR	Raman	INS	[a]Assignment
		56-80	Water – acoustic modes
		155	Water – acoustic modes
		160	Lipids (membranes) – $\tau(CH_3)$
		224	Water – H-bonded (weak)
		240	Proteins – $\tau(CH_3)$
		290	Proteins – $\tau(CH_3)$
		304	Water – H-bonded (strong)
		540-1100	Water – librational modes
		560	Water – intracellular
	720	728	B-DNA (A,T) – $\nu(CC)_{ring}$
	780-785		B-DNA (C,T,U) – $\nu(CC)_{ring}$ B-DNA – $\nu(OPO)_{backbone}$
	830-850		B-DNA – $\nu(OPO)_{backbone}$ Proteins (Pro,Trp,Tyr) – $\nu(CC)$, $\delta(CCH)$ Polysaccharides – $\gamma(COC)$
863			Tyr – $\nu(CC)_{ring}$
	920		B-DNA (deoxyribose) – $\nu(CC)_{ring}$
980			Proteins (phosphorylated) – $\nu(OPO)$
1003	1003		Proteins (Phe) – $\nu_s(CC)_{ring}$
	1033		Phospholipids – $\delta(CCH)$
1080-1090	1070-1090		B-DNA, RNA – $\nu_s(PO_2^-)$ Proteins – $\nu(CC)$, $\nu(CN)$ Phospholipids – $\nu_s(PO_2^-)$ Glycogen – $\nu(CC)$, $\nu(CO)$
1139	1128		RNA (ribose) – $\nu(CO)$ Proteins – $\nu(CN)$ Lipids – $\nu(CC)_{acyl}$ Carbohydrates – $\nu(CO)$, $\nu(CC)$
1170	1170		DNA (C,G,T) – $\nu(CC)_{ring}$ Proteins (Phe,Trp,Tyr) – $\delta(CH)$
1235-1245	1235-1245		Lipids, carbohydrates – $\delta(CH_2)$, $\omega(CH_2)$, $t(CH_2)$ B-DNA, RNA – $\nu_{as}(PO_2^-)$
	1250		Proteins – amide III (δ(CN–H)/ν(CN))
	1314	1350	DNA (A,G) – $\nu(CC)_{ring}$, $\delta(CH)$ Proteins (Trp) – $\nu(CC)_{ring}$, $\delta(CH_2)$
1400-1450	1400-1450	1430-1470	Proteins, lipids, carbohydrates – $\delta(CH_2)$; $\delta(CH_3)$ membranes
1550-1560	1555		Proteins – amide II (δ(CN–H)/ν(CN))

			DNA (G) – $\nu(CC)_{ring}$
1585	1585		DNA (T) – $\nu(CC)_{ring}$ Proteins (Phe,Trp) – ν(C=C), ν(C=N)
	1622	1620	Water – δ(OHO)
1650-1660	1650-1660		DNA – $\delta(NH_2)$ Proteins – amide I (ν(C=O)) Lipids – ν(C=C)
1740			Phospholipids ($\nu(C=O)_{ester}$)
2850-2875	2850		Proteins, lipids, carbohydrates – $\nu_s(CH)$, $\nu_s(CH_2)$
2880	2880-1890		Proteins, lipids, carbohydrates – $\nu_s(CH_3)$
2900-2935	2933		Proteins, lipids, carbohydrates – $\nu_{as}(CH_2)$
2960	2960		Proteins, lipids, carbohydrates – $\nu_{as}(CH_3)$
	3060		Proteins – amide B (2×amide I FR ν(NH))
3250-3300	3300		Proteins – amide A (ν(NH))
3300-3400			Lipids, carbohydrates – ν(OH)
3450	3450		Water – ν(OH)

[a]A – adenine; C – cytosine; dG – deoxyguanine; dT – deoxythymine; G – guanine; Glu – glucose; Hyp – hydroxyproline; Met – methionine; Phe – phenylalanine; Pro – proline; T – thymine; Trp – tryptophan; Tyr – tyrosine; U – uracil; Val – valine. δ – in-plane deformation; γ – out-of-plane deformation; ν – stretching; ρ – rocking; t – twisting; ω – wagging. s – symmetric; as – anti-symmetric; FR – Fermi resonance.

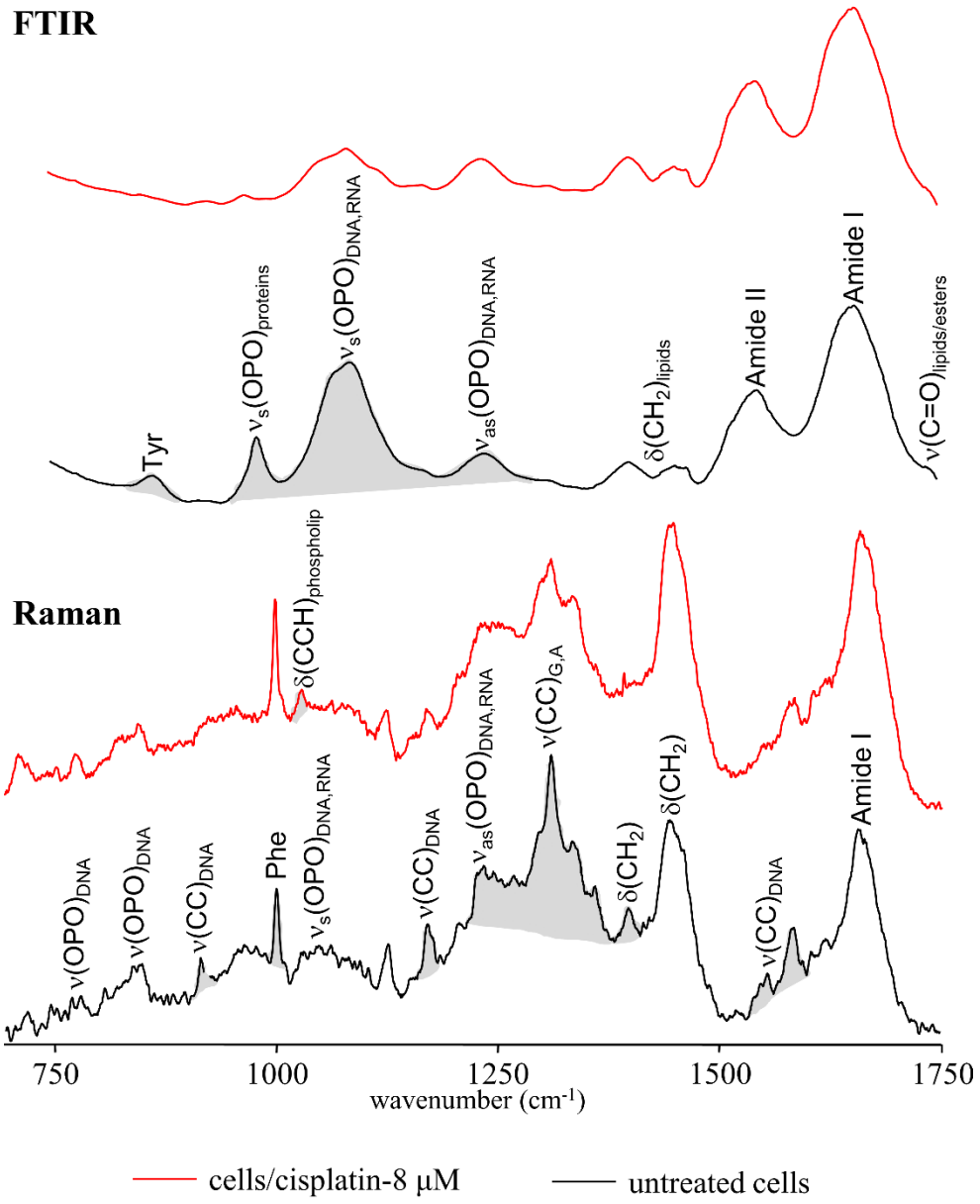

Fig. S1 Raman and FTIR spectra (at room temperature) of lyophilised MDA-MB-231 cells, both untreated and cisplatin-treated/8 µM.

(The most significant spectral changes are shaded in grey).

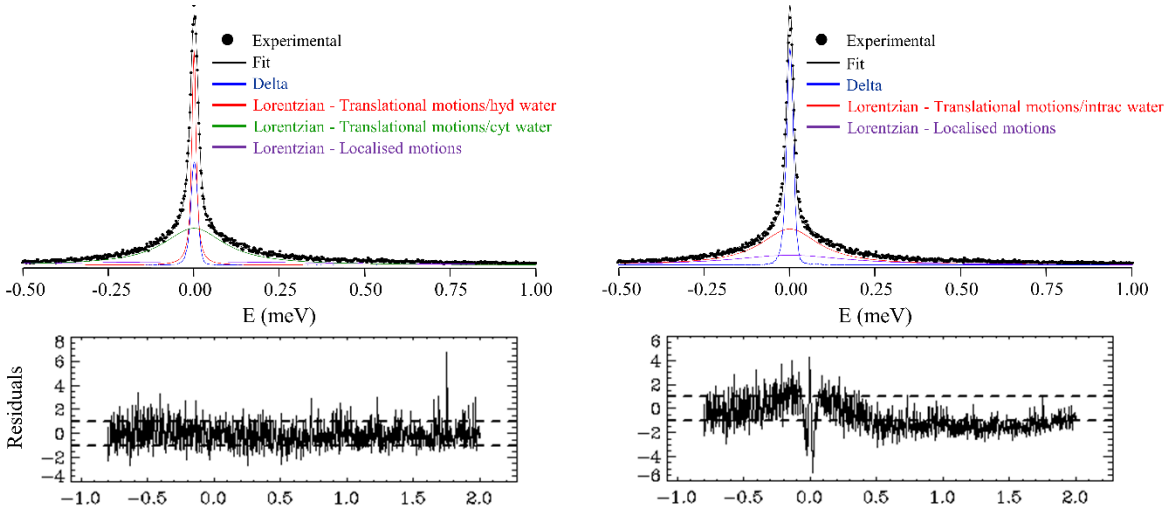

Fig. S2 QENS spectra (at 298 K) at Q=1.079 $Å^{-1}$for untreated MDA-MB-231 cells in deuterated saline medium (washed), fitted using: (A) two Lorentzian and one Delta functions. (B) three Lorentzian and one Delta functions.
(The corresponding residual plots are shown).