## Electronic Supplementary Information

Binding kinetic experiments

The kinetics of interaction between **I** and holo-transferrin was studied under simulated extracellular conditions. Samples of 2.5×10^{-5} or 1×10^{-4} M **I** and 5×10^{-5} M protein (1:2 and 2:1 ratios) were incubated in 10 mM phosphate buffer containing 100 mM sodium chloride, pH 7.4 at 37°C. Aliquots of the reaction mixture were continuously taken for CE-ICP-MS analysis to monitor the time-dependent changes in the peak areas of Ru-containing species (see Figure 2). To visualize these changes, Figure S-1 is given. The reaction rate constant (k) was assessed from the polynomial approximation of the adduct response vs. time plot by assuming the first-order character of the binding reaction, *i.e.*, the validity of an equation:

$$\ln \frac{X_{drug}^{bound}}{C_{drug}^{0}} = -kt$$

where X_{drug}^{bound} is the relative adduct signal area (adduct peak area divided on the sum of all peak areas) and C_{drug}^{0} represents the initial concentration of the drug. The validity of this assumption has been previously confirmed in similar kinetic measurements (see ref 15).
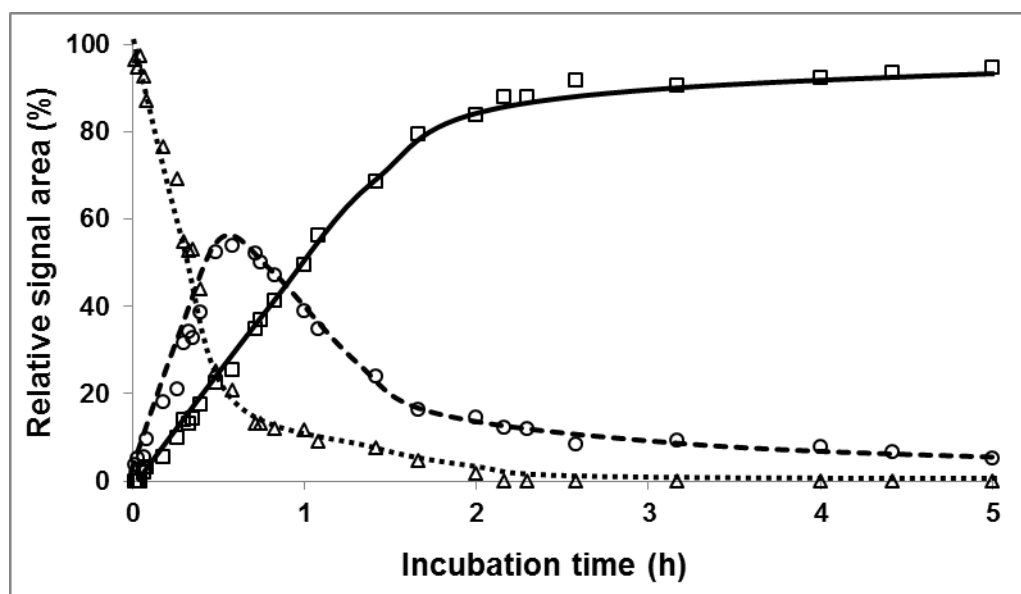
Figure S-1. Evolution of the Ru–holo-transferrin adduct (squares), **I** (triangles), and the intermediate product (circles) concentrations at a ruthenium-to-protein ratio of 2:1.

Table S-1   ICP-MS instrumental/operating parameters[a]

Parameter	Setting
generator output power, W	1250
nebulizer	PolyCon
nebulizer chamber	quartz, cooling at 3^oC
flow-rate of plasma-forming argon, L/min	13
flow-rate of auxiliary argon, L/min	0.9
flow-rate of argon into atomizer, L/min	0.95
flow-rate of the analyzed sample, mL/min	0.8
resolution, M	0.7
dwell time, ms	0.6
number of runs	10
channels per mass	10

[a] X-7, Thermo Elemental, USA.

Table S-2   Typical levels of the components of reaction mixtures

Component	Concentration (M)[a]
I	$5 \times 10^{-6} - 1.5 \times 10^{-4}$ (1×10^{-4})
transferrin	4×10^{-5} (5×10^{-5})
glutathione	$5 \times 10^{-4} - 1 \times 10^{-2}$ (1×10^{-2})
ascorbic acid	0.01 (0.01)
citric acid	0.05– 0.1 (0.05)

[a] Given in parentheses is the concentration chosen for this study.