Supporting Information

Ultrasensitive, Selective and Simultaneous Detection of Cytochrome C and Insulin Based on Immunoassay and Aptamer-based Bioassay in Combination with Au/Ag Nanoparticle Tagging and ICPMS Detection

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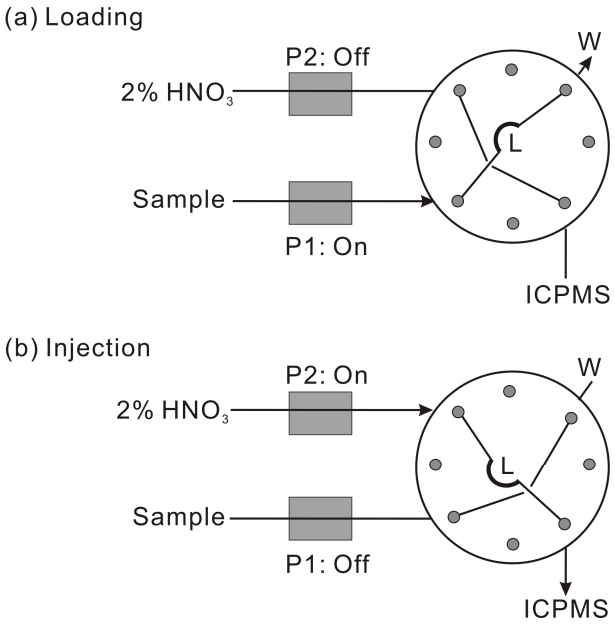

Fig. S1. FI manifold and operational sequence for sample injection to ICPMS, P1 and P2, peristaltic pumps; L, loop, 25 μL; W, waste. Valve position: (a) loading, (b) injecttion.

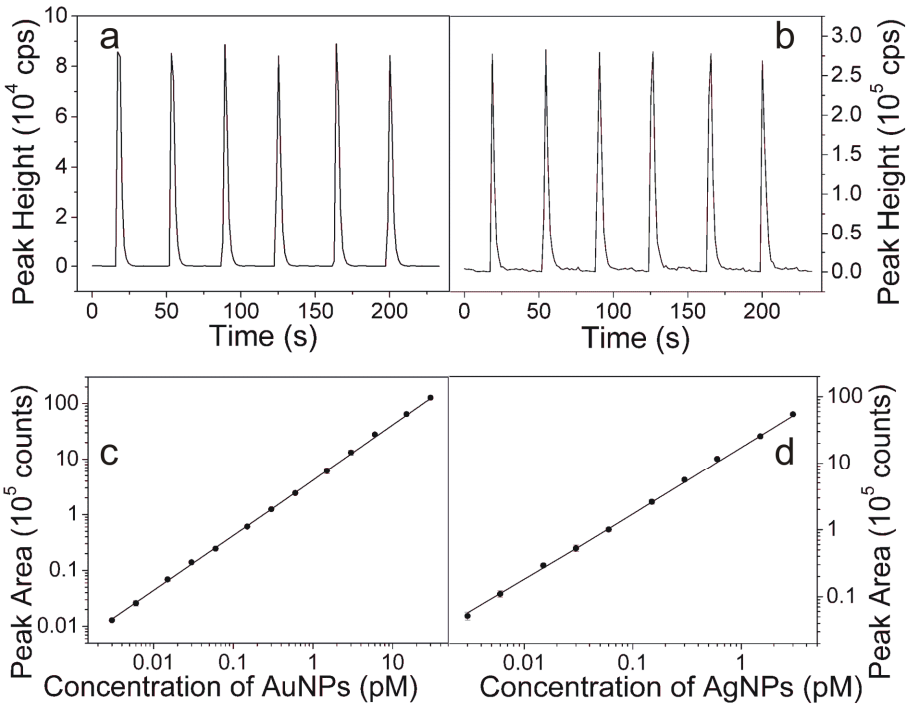

Fig. S2. Reproducible FI-ICPMS response for 1.5 pM AuNPs (a) and 0.6 pM AgNPs (b); The calibration curves obtained from the FI-ICPMS analyses of 25 μL solutions containing various concentrations of AuNPs (0.003-30 pM) (c) and AgNPs (0.003-3 pM) (d). The results were average from six replicate ICPMS analyses.

Table S1. Optimized Operational Conditions and Mass Spectrometer Settings for the X Series ICPMS

ICPMS instrument	Thermo Elemental X7 Series
RF power	1200 W
Plasma gas flow	13.5 L min^{-1}
Auxiliary gas flow	0.95 L min^{-1}
Nebulizer gas flow	0.83 L min^{-1}
Sample uptake rate	1.2 mL min^{-1}
Resolution	Standard
Dwell time	600 ms
Integration mode	Peak area
Isotopes monitored	^{197}Au, ^{107}Ag

Table S2. Contents of C, H, and N in the Prepared MMPs and Silica-Coated MMPs, and Amine-Functionalized MMPs with Surface Modification by APTES under Different Experimental Conditions.

			element content (wt %)		
	reaction solvent	temperature	C	H	N
MMPs	—	—	0.42	2.22	0.19
silica-coated MMPs	—	—	1.91	3.68	0.27
amine-functionalized	EtOH	RT	2.91	0.99	0.33
MMPs	EtOH/H_2O (1/1, v/v)	RT	3.02	1.02	0.40
	EtOH/H_2O (1/1, v/v)	60℃	3.99	2.27	1.01
	DMF/Toluene (3/2, v/v)	RT	2.37	1.19	0.62
	DMF/Toluene (3/2, v/v)	60℃	2.90	0.74	0.93

Table S3. Comparison of our element-tagged ICPMS assay with other developed methods for insulin with respect to limit of detection (LOD), and linear dynamic range (LDR)

Methods	LOD	LDR	Ref.
electrochemistry (amperometry)	500 nM	NA[a]	(1)
electrochemistry (FIA)	50 nM	100 nM – 1 μM	(2)
electrochemistry (amperometry)	30 nM	100 – 3 μM	(3)
electrochemistry (FIA[b])	23 nM	100 nM – 1 μM	(4)
electrochemistry (amperometry)	20 nM	50 nM – 500 nM	(5)
electrochemistry (FIA)	14 nM	100 nM – 1 μM	(6)
electrochemistry (FIA)	2 nM	6 nM – 400 nM	(7)
imaging ellipsometry based immunoassay	2 nM	2 nM – 20 μM	(8)
electrochemistry (FIA)	1 nM	10 nM – 80 nM	(9)
electrochemistry (amperometry)	0.45 nM	0.5 nM -- 500 pM	(10)
electrochemistry (amperometry)	0.4 nM	0.5 nM – 850 nM	(11)
SPR immunosensor	0.2 nM	0.2 nM – 60 nM	(12)
element-tagged ICPMS assay	110 pM	0.4 nM – 40 nM	This work
electrochemistry (amperometry)	40 pM	100 pM – 700 nM	(13)
electrochemistry (FIA)	40 pM	100 pM – 500 pM	(10)
electrochemistry (amperometry)	22 pM	100 pM – 4 μM	(14)
electrochemistry (FIA)	2.6 pM	15 pM –100 pM	(13)
liposomal immunosensor	1.36 pM	10 pM – 10 nM	(15)
electrochemistry (FIA)	NA	8.2 to 81.6 ng in 7.5 μL	(16)

[a] not available; [b] Flow injection analysis.

Table S4. Comparison of our element-tagged ICPMS assay with other developed methods for cyt-c with respect to limit of detection (LOD), and linear dynamic range (LDR)

Methods	LOD	LDR	Ref.
capillary electrophoresis	3.4 μM	1 μM – 600 μM	(17)
electrochemical method	1 μM	5 μM – 300 μM	(18)
electrochemical method	0.5 μM	1 μM – 100 μM	(19)
gold nanoparticle amplified electrochemistry	0.67 nM	2 nM – 100 nM	(20)
electrochemical method	0.2 nM	0.4 nM – 1.2 μM	(21)
spectrofluorimetric method	67 pM	0.3 nM – 9.2 nM	(22)
element-tagged ICPMS assay	30 pM	0.1 nM – 20 nM	This work
enzyme-linked immunosorbent assay	7.7 pM	7.7 pM – 77 nM	(23)

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