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ARTICLE TYPE

Supporting information

Ferritin nanocages loaded with gold ions induce oxidative stress and apoptosis in MCF-7 human breast cancer cells

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5 **Figure S1**. Photo of the solutions of **Au_2phen** -encapsulated AFt, **Auoxo4-**encapsulated AFt and of **Auoxo3**-encapsulated AFt.

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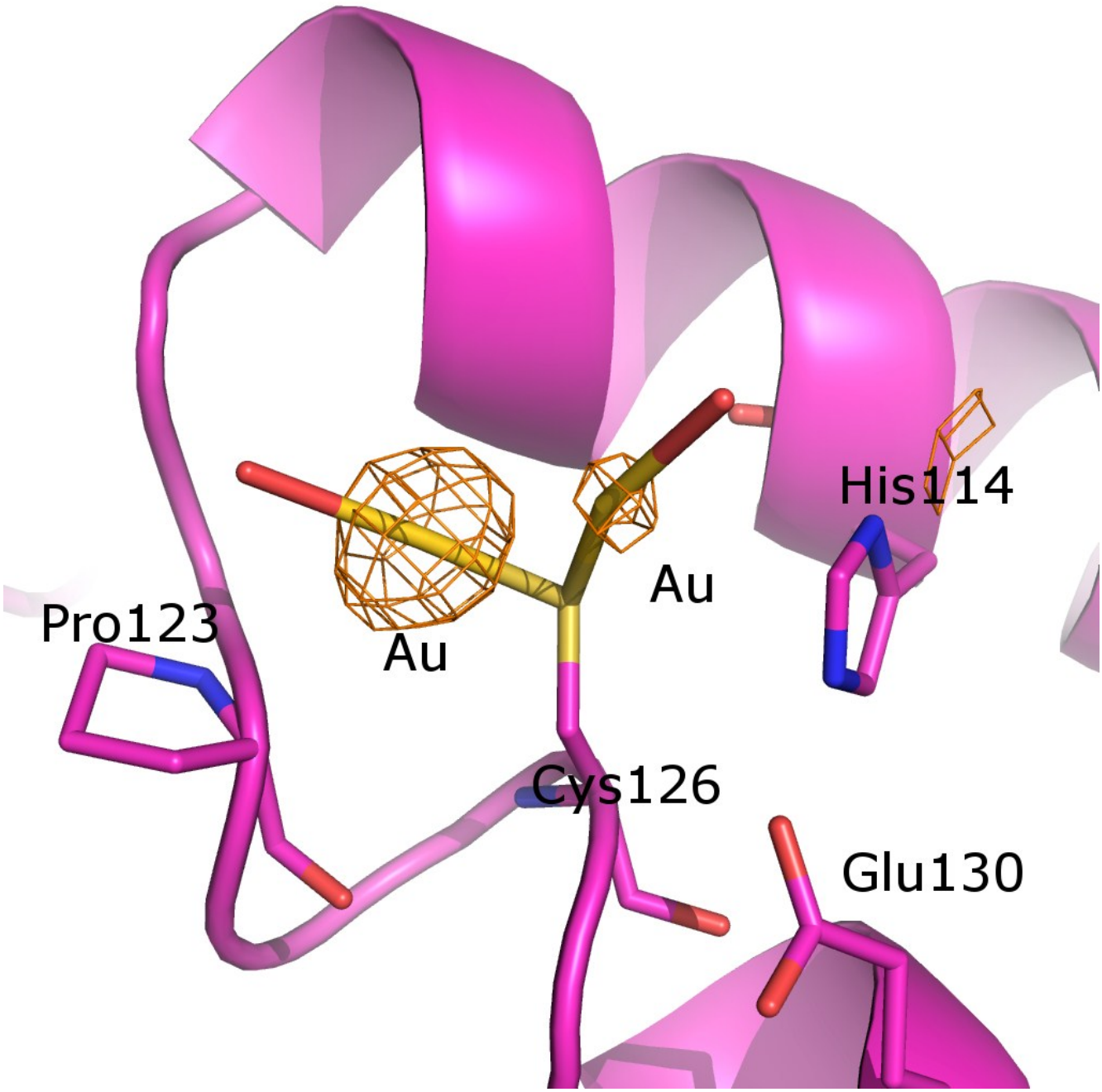
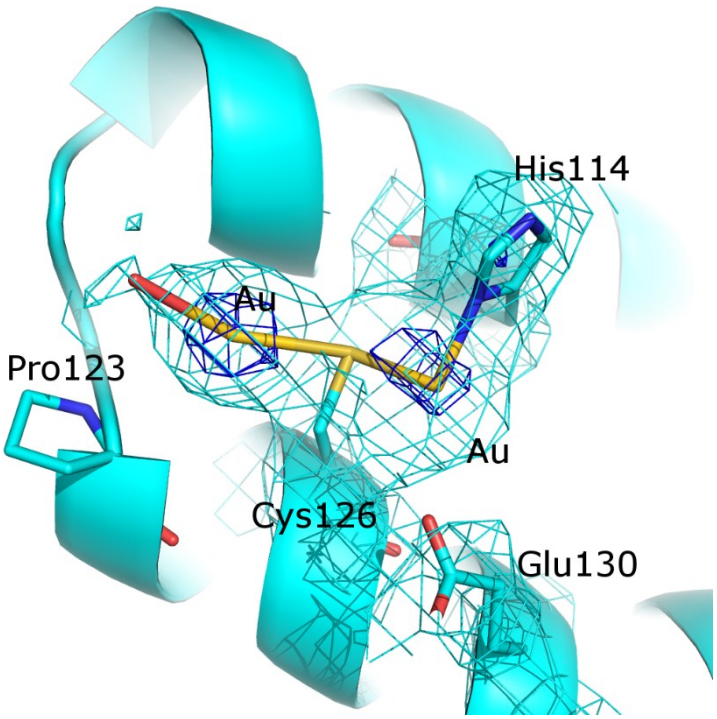
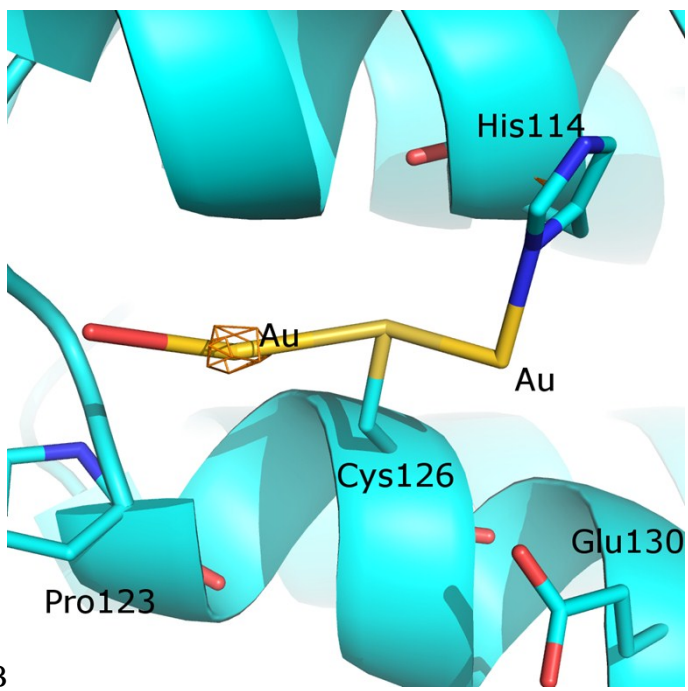


Figure S2. Gold binding site region in **Au_2phen**-encapsulated AFt. Bijvoet difference Fourier map calculated with anomalous data and reported at 4 σ.


His114
Au
Pro123
Au
Cys126
Glu130

A


His114
Au
Au
Cys126
Glu130
Pro123

B

Figure S3. Gold binding site region in **Auoxo4**-encapsulated AFt. 2Fo-Fc electron density maps are reported at 0.8 σ (cyan) and 4 σ (blue). Bijvoet difference Fourier map calculated with anomalous data and reported at 3 σ is in orange in panel B.

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Table S1. Data collection and refinement statistics

	Au_2phen-encapsulated AFt	**Auoxo4**-encapsulated AFt
Data Collection statistics X-ray source	Rotating anode	Rotating anode
Wavelength	λ=1.5418Å	λ=1.5418Å
Space group	F432	F432
Unit-cell parameters a=b= c (Å), α,β,γ (°)	180.97 90	180.88 90
Ft Monomers per a. u.	1	1
Resolution (Å)	104.5-1.82 (1.85-1.82)	104.4-2.60 (2.64-2.60)
Observed reflections	287733	32931
Unique reflections	23324	8209
Completeness (%)	99.9 (100)	99.0 (99.7)
Rmerge	0.121 (0.680)	0.187 (0.414)
Rpim	0.126 (0.269)	0.145 (0.401)
I/σ(I)	11.9 (3.2)	5.4 (2.9)
Multiplicity	12.3 (7.2)	4.0 (4.1)
CC1/2	0.857	
Refinement		
Resolution (Å)	104.5-1.82	104.4-2.60
n. of reflections in working set	22173	7881
n. of reflections in test set	1138	391
R factor/Rfree (%)	14.3/17.2	18.4/23.6
n of non-H atoms in the refinement	1822	1605
Occupancy of Au ions	0.50, 0.30	0.50, 0.35
B-factor of Au ions ($Å^2$)	16.9, 48.1	41.5, 47.1
Overall B-factor	18.6	23.6
Deviations from ideality values R.m.s.d. bonds (Å)	0.022	0.013

R.m.s.d. angles (Å)	1.86	1.47

Table S2. Comparison of anomalous peak intensity of the most representative Cd ions, i.e. those conserved in the structures of AFts, in **Au2phen-**, **Auoxo4-** **Auoxo3-**encapsulated AFts and in the structure of CDDP- and CBDCA-encapsulated AFts, used as control. Only data collected using CuKα are compared.

	Auoxo4-encapsulated AFt	Au2phen-encapsulated AFt	Auoxo3-encapsulated AFt	CDDP-encapsulated AFt	CBDCA-encapsulated AFt
Source Resolution PDB code	CuKα λ=1.5418 Å 2.6 Å	CuKα λ=1.5418 Å 1.82 Å	CuKα λ=1.5418 Å 1.96 Å 5IX6	CuKα λ=1.5418 Å 2.06 Å	CuKα λ=1.5418 Å 1.96 Å 5MIK
Atom in 5ERK					e/Å^3
CD 1. Close to Glu11	<0.10	0.23	0.22 (CD8)	0.24	0.22
CD 2. Close to Glu53/Glu56	<0.10	0.16	0.21(CD9)	0.16	0.22
CD 3. Close to Glu60	<0.10	0.28	0.20 (CD15)	0.31	0.25
CD 4. At the binary axis. Close to Asp80	<0.10	1.80	1.19 (CD10)	0.92	1.08
CD 5. Close to Glu88	Absent	0.10	<0.10	<0.10	0.12
CD 6. Close to Asp127		0.10	<0.10	0.35	<0.10
CD 7. Close to His132	0.13	0.23	0.25(CD11)	0.28	< 0.10 (0.17 using λ=0.97Å) **Interpreted as Pt**
CD 8. At the ternary axis. Close to Glu130	0.30	0.51	0.58 (CD12)	0.41	0.39
CD 9. Close to His114 and at 3.7 from Cys126	<0.10	<0.10	0.19	0.25	0.08/0.09
Atoms in 5IX6					
Au1 close to SG Cys126 and His114	Absent	Absent	0.76 **Interpreted as Au**	<0.10	
Au2 close to Cys48 (and Close to Arg52)	E.d. absent <0.1	E.d. absent <0.1	0.37 **Interpreted as Au**	<0.10	0.16 **Interpreted as Cd**
Au3 close to His49	<0.10	< 0.10 Interpreted as water	0.52 **Interpreted as Au**	<0.10	0.04/0.13 (0.17 using λ=0.97Å) **Interpreted as Pt**
Au4 close to SG Cys126	0.22 **Interpreted as Au**	1.06 **Interpreted as Au**	1.00 **Interpreted as Au**	<0.10	-
Au5 close to His147	-	< 0.1 Interpreted as water	**Interpreted as Au** 3.14	<0.10	-
CD 11. Close to Cys48	<0.10	0.16 Interpreted as Cd	0.50 **Interpreted as Au6** close to Cys48 (and close to His49	0.25 Interpreted as Cd	0.16 Interpreted as Cd

Au7 close to His132	E.d. absent <0.10	E.d absent <0.1	**Interpreted as Au** 0.16	0.21 **Interpreted as Pt**	
Au close to Cys126	**Interpreted as Au** 0.13	**Interpreted as Au** 0.23	Interpreted as water. Close to Au1	<0.10	
CD16	<0.10	Interpreted as water <0.10	0.21	Absent Close to Asp53	

Table S3.Uninterpreted peaks of electron density in the Fo-Fc map:

Auoxo4-encapsulated AFt

	e/Å^3	Reason
Peak 1	0.81	Too close to SG atom of Cys126, CL and Au atoms
Peak 2	0.80	In the middle oft he nanocage. Not bound tot he protein
Peak 3	0.68	Too close to side chain of His149
Peak 4	0.60	Too close to CD20 and wat 266
Peak 5	0.59	Too close to side chain of Arg153
Peak 6	0.56	Too close to side chain of His149
Peak 7	0.51	Too close to CD1

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Au_2phen-encapsulated AFt

	e/Å^3	Reason

Peak 1	0.81	Too close to gold atom and SG atom of Cys126
Peak 2	0.80	Too close to a water molecule
Peak 3	0.68	Too close to side chain of Gln79
Peak 4	0.60	Too close to side chain of Glu163
Peak 5	0.59	
Peak 6	0.56	
Peak 7	0.51	