## **Supporting Information**

Internalization of a Preformed Atomically Precise Silver Cluster in Proteins by Multistep Events and Emergence of Luminescent Counterparts Retaining Bioactivity

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## Protocol for the synthesis of [Ag<sub>18</sub>HSA]:

25 mg HSA was dissolved in 1.6 mL Milli-Q water. Then stirred the solution for 1 min. Under stirring condition, 400  $\mu$ L of I was added. The addition of I into the HSA solution made the reaction mixture turbid. The turbid solution was centrifuged after 12 h and from the supernatant the brown colored cluster solution was collected. This solution was used for characterization.

## Protocol for the synthesis of [Ag<sub>13</sub>Lf]:

25 mg Lf was dissolved in 1.6 mL Milli-Q water. Then stirred the solution for 1 min. Under stirring condition, 400  $\mu$ L of I was added. The addition of I into the Lf solution made the reaction mixture turbid. The turbid solution was centrifuged after 12 h and from the supernatant the brown colored cluster solution was collected. This solution was used for characterization.



**Figure S1:** The EDS spectrum of the precipitate along with the quantification data (A). (B) is the image of the precipitate under visible light (left) and under UV light (right).



**Figure S2:** The EDS spectrum of the  $Ag_{18}$ @BSA cluster along with the quantification data (A). (C–E) are the EDS images of the cluster collected using Ag La, S Ka, and N Ka emissions. Corresponding SEM image of the Ag\_{18}@BSA is shown in B. The quantification data suggest that the Ag:S ratio is in good agreement with the theoretical value for Ag\_{18}@BSA.



**Figure S3:** Total XPS survey spectrum of  $Ag_{18}$ @BSA. The insets show the spectra of the cluster in the Ag 3d region and S 2p regions.



**Figure S4:** Characterization of the Ag<sub>18</sub>@HSA cluster. (A) UV-vis profile of HSA (blue trace) and Ag<sub>18</sub>@HSA cluster (red trace). (B) Luminescence profile of the Ag<sub>18</sub>@HSA cluster. Inset shows the color of HSA and the cluster under visible light (top) and under UV light (bottom).



**Figure S5:** MALDI MS of pure HSA (blue trace) collected in linear positive ion mode using sinapic acid as matrix and that of the as-prepared red emitting  $Ag_{18}$ @HSA (red trace).



**Figure S6:** Characterization of  $Ag_{13}$ @Lf cluster. (A,B) UV-vis and luminescence spectra (excitation at 365 nm) of  $Ag_{13}$ @Lf cluster. C) MALDI MS spectra of the parent protein and the cluster showing the formation of the  $Ag_{13}$ @Lf cluster.

Table S1: Nur	mber of cystein	e/methionine, Tr	p/Tyr/His, and	disulfide b	oridges pre	esent in	BSA,
HSA, and Lf.							

	Cys (C)	Met (M)	Trp (W)	Tyr (Y)	His (H)	Disulfide
						bond
BSA	35	5	2	19	17	17
HSA	35	5	1	16	17	17
Lf	33	3	13	19	10	16

Note: Though the molecular weight of Lf is high than BSA and HSA, the number of His residue present in Lf is less. Thus the ability of Lf to stabilize the small clusters formed at initial stage is expected to be lower than both BSA and HSA. This probably result in the formation of a smaller 13-atom Ag cluster in this case.



Figure S7: Time dependent luminescence profile of the Ag<sub>18</sub>@BSA cluster during synthesis.



**Figure S8:** UV-vis profile of Ag nanoparticle formed in a reaction of  $[Ag_{18}H_{16}(TPP)_{10}]^{2+}$  cluster with reduced concentration of protein.



**Figure S9:** (A) MALDI MS of BSA before (blue) and after (red) reaction with Ag Nps. The presence of conalbumin in the BSA solution is indicated with an asterisk (\*). (B) UV-vis spectrum of Ag Nps.



**Figure S10:** The viability of HeLa cells after treating with different concentrations of  $Ag_{18}$ @BSA NCs for 24 hours. The viability was obtained by resazurin assay. The error bar represents standard error of 3 trials.



**Figure S11:** Microscopic images of the HeLa cells after 5 h incubation with NCs. (A) Fluorescence image of NCs in cells (B) Cell nucleus stained with DAPI. (C) Bright-field image of the corresponding fluorescence images. (D) An overlay of these three images.



Figure S12: Z stacking images of cells shows the internalization of NCs in the HeLa cells.



**Figure S13:** Phosphatase activity of pure Lf and Ag<sub>13</sub>@Lf clusters as a function of time. Cluster showed 90% catalytic activity.