Supporting Information

Active Regulation of Protein Corona for Enhancing the *in vivo* Biodistribution and Metabolism of Nanoparticles

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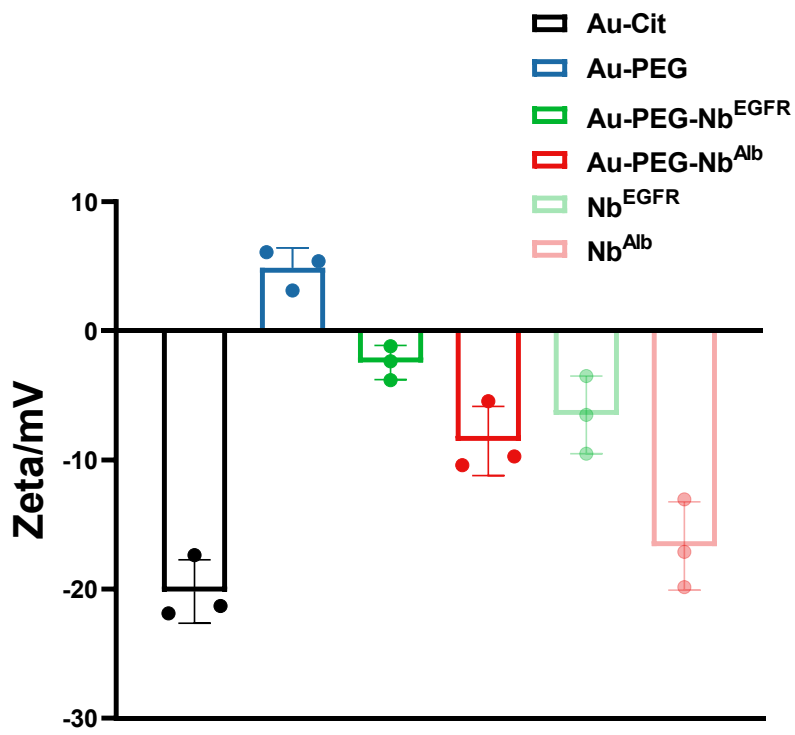

Figure S1. The zeta potential of Au-Cit, Au-PEG, Au-PEG-Nb^{EGFR}, Au-PEG-Nb^{Alb}, Nb^{EGFR} and Nb^{Alb}.

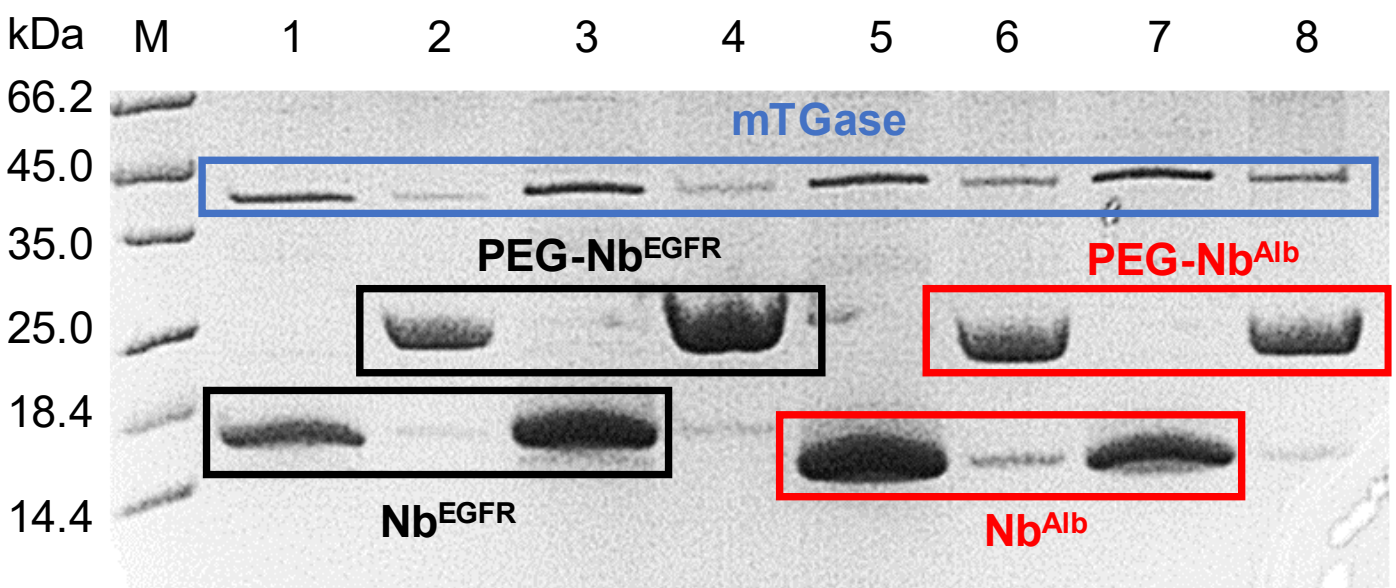

Figure S2. SDS-PAGE analysis of the Nb conjugation reaction with Au-PEG. The supernatant from the Au-PEG-Nb conjugation reaction (lanes 1 and 3 for Nb^{EGFR}, and lanes 5 and 7 for Nb^{Alb}), and the released PEG-Nb from the Au-PEG-Nb conjugates (lanes 2 and 4 for PEG-Nb^{EGFR}, and lanes 6 and 8 for PEG-Nb^{Alb}). The samples in lanes 1, 3, 5 and 7 are the supernatant obtained after incubation of Au-PEG with nanobodies and mTGase, which contains excess unreacted nanobodies (15-16 kDa) and mTGase (38 kDa). In contrast, samples in lanes 2, 4, 6 and 8 are PEG-Nb released from·Au-PEG-Nb·by DTT·reduction and thus show significantly fewer mTGase bands at 38 kDa compared to lanes 1, 3, 5 and 7 with most bands corresponding to PEG-Nb.

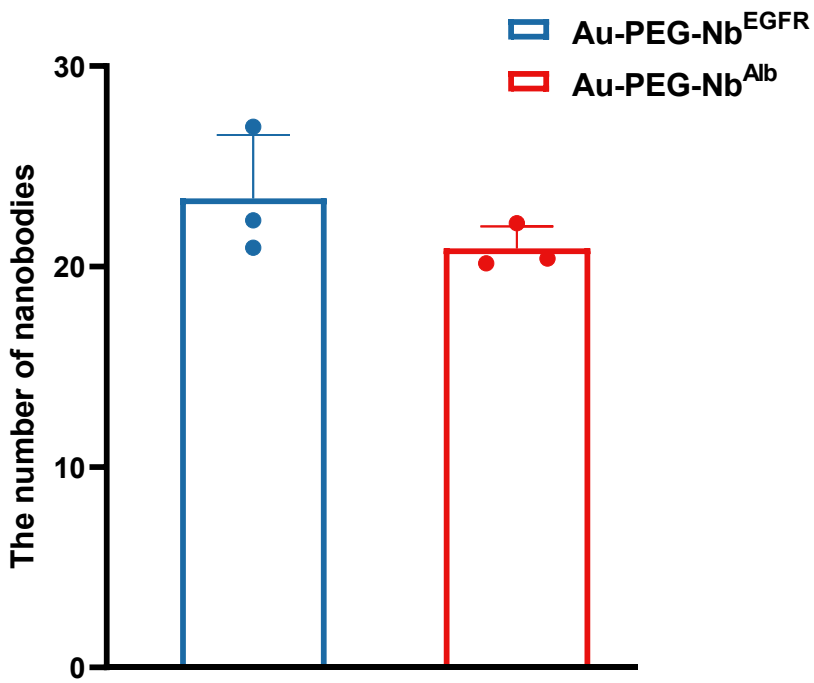

Figure S3. The content of nanobodies on Au-PEG-Nbs was measured by BCA assay. The absorbance was used to calculate the concentration of gold nanoparticles with a 13 nm diameter using a $\varepsilon = 2.7 \times 10^8\ M^{-1}cm^{-1}$ extension coefficient at 520 nm with the Beer-Lambert law.

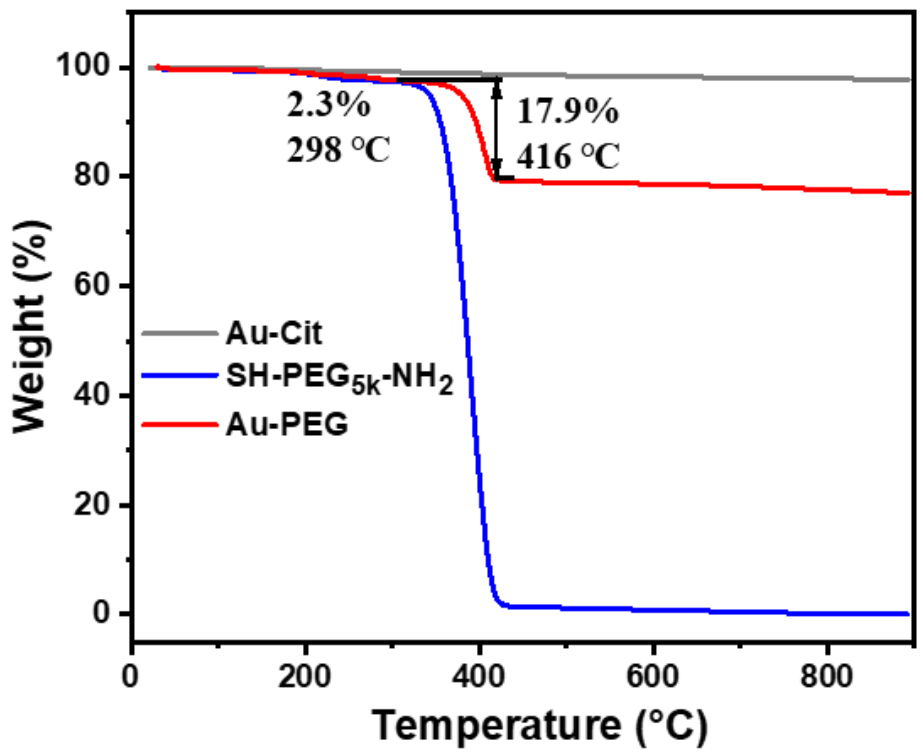

Figure S4. Thermogravimetric analysis (TGA) was used to measure the weight loss of SH-PEG_{5k}-NH_2, Au-Cit, and Au-PEG as a function of temperature.

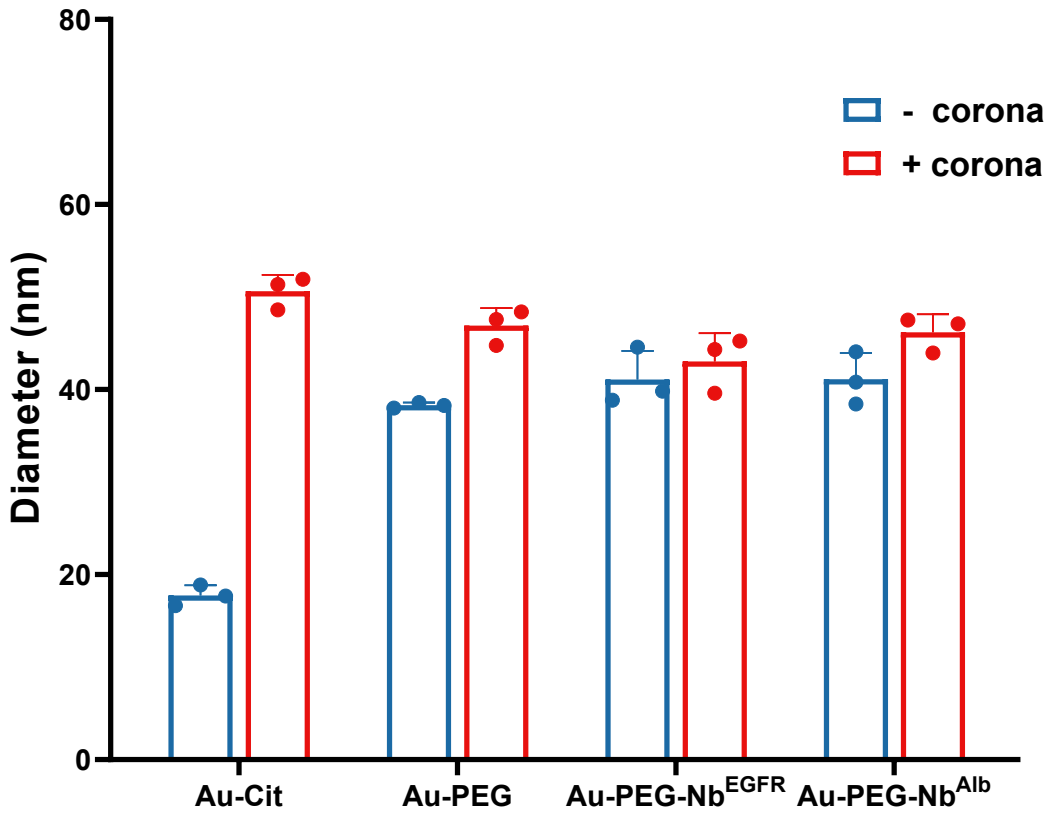

Figure S5. The change in diameter of the AuNPs before and after the formation of the protein corona.

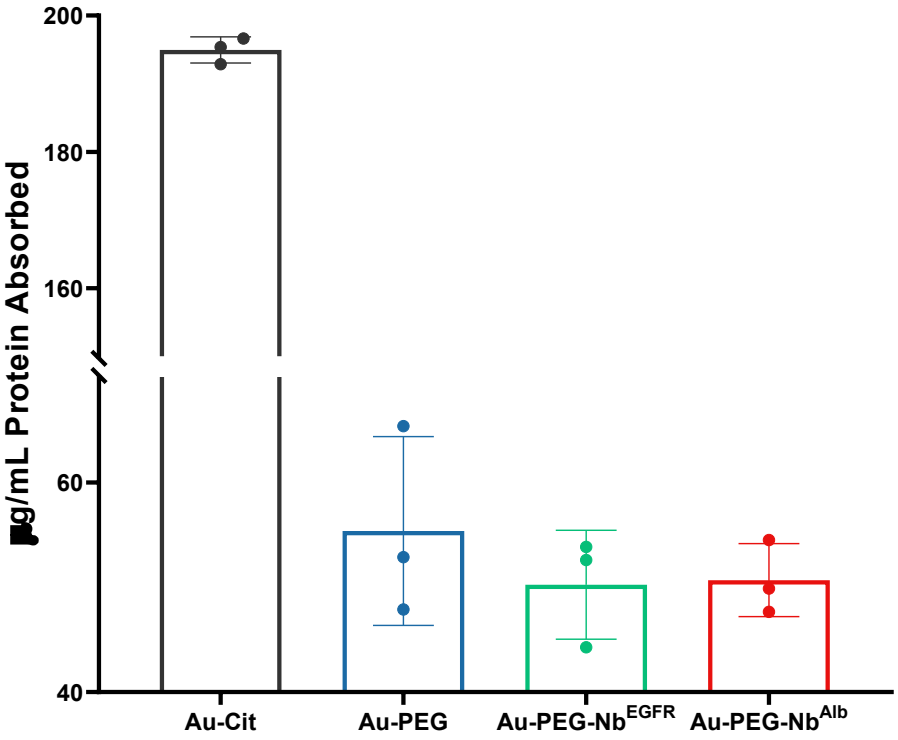

Figure S6. The content of protein corona on AuNPs was determined by BCA assay. We simultaneously prepared two samples of Au-PEG-Nbs. One portion was used to measure the protein content of Nbs on the surface of Au-PEG-Nbs, while the other portion was incubated with FBS to form a protein corona. Subsequently, the protein content of all surface proteins on Au-PEG-Nbs was determined. The difference between these two measurements represents the protein content of the surface protein corona.

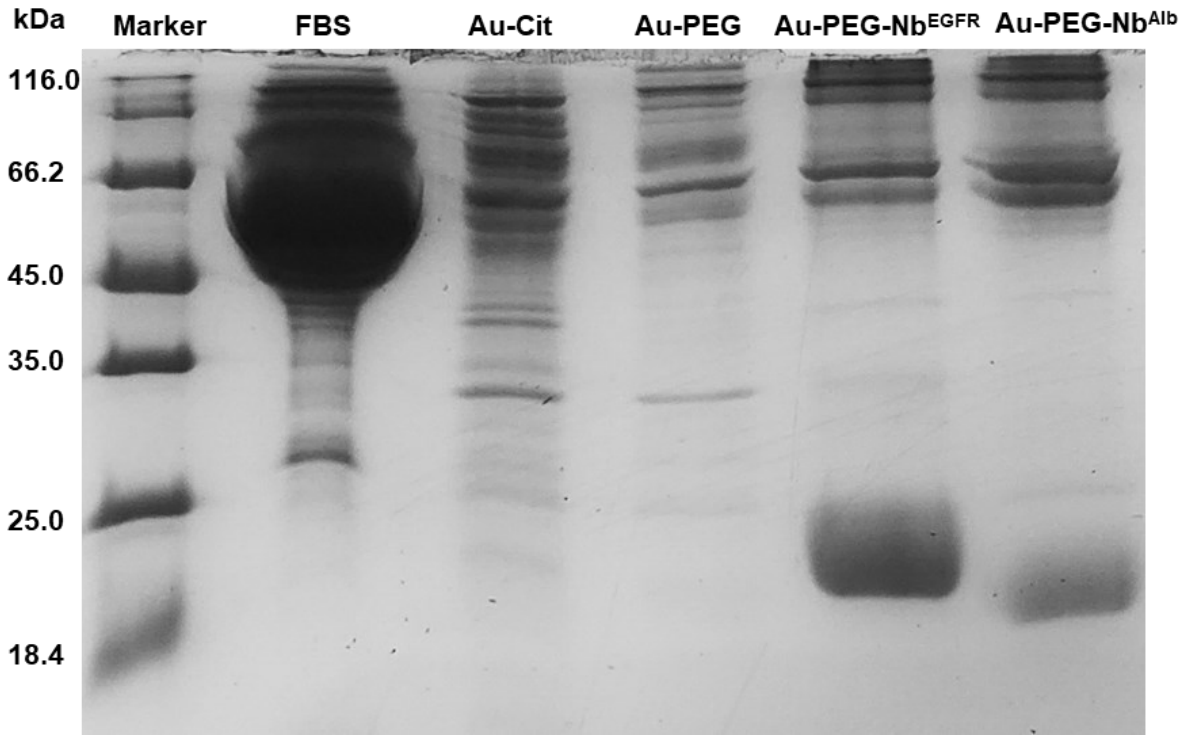

Figure S7. The SDS-PAGE analysis the protein corona of AuNPs in FBS.

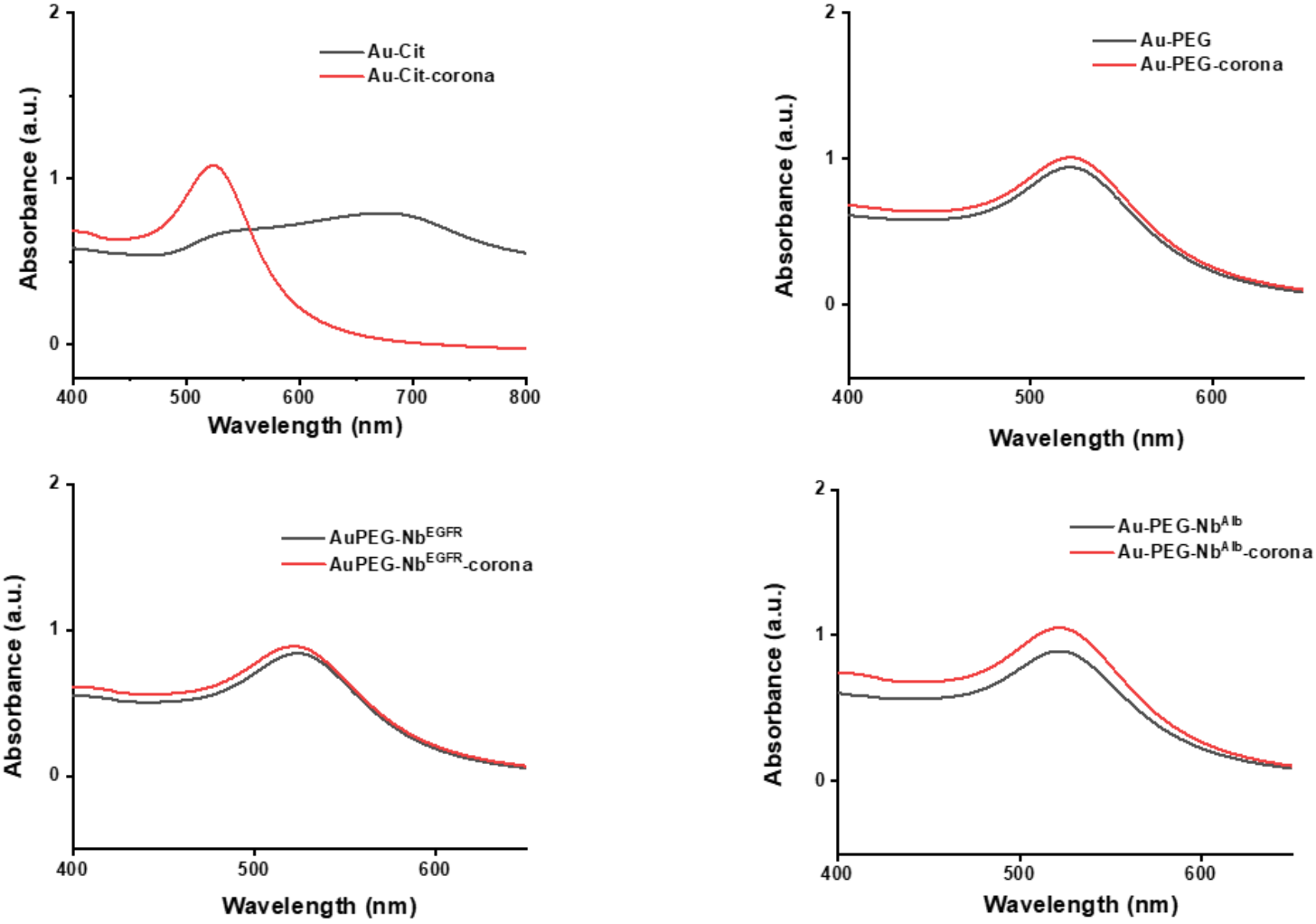

Figure S8. Summary of UV/vis spectra of AuNPs before and after protein corona formation.

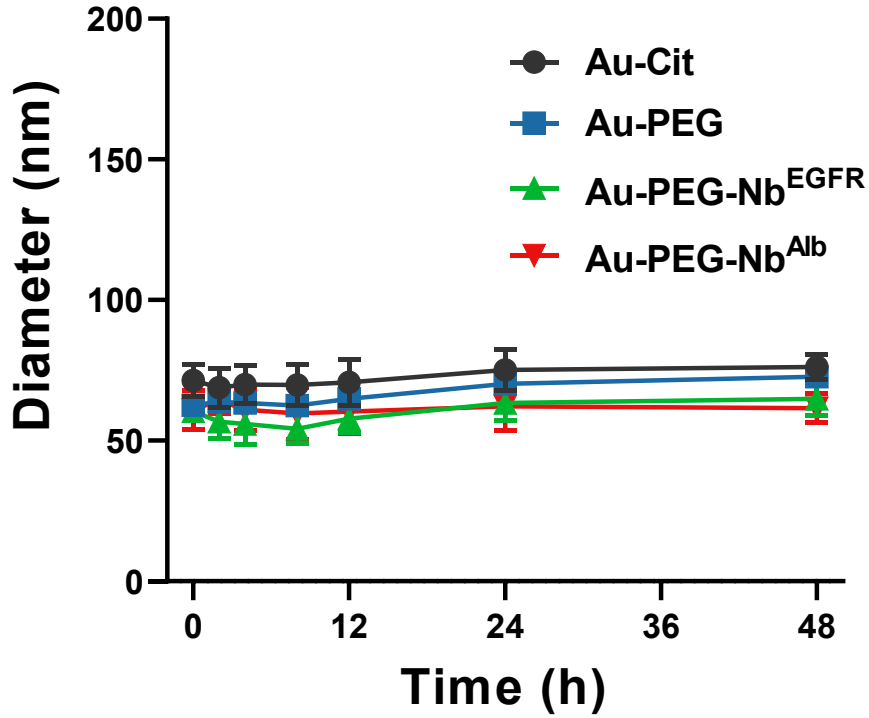

Figure S9. The stability of AuNPs in serum during 48 h.

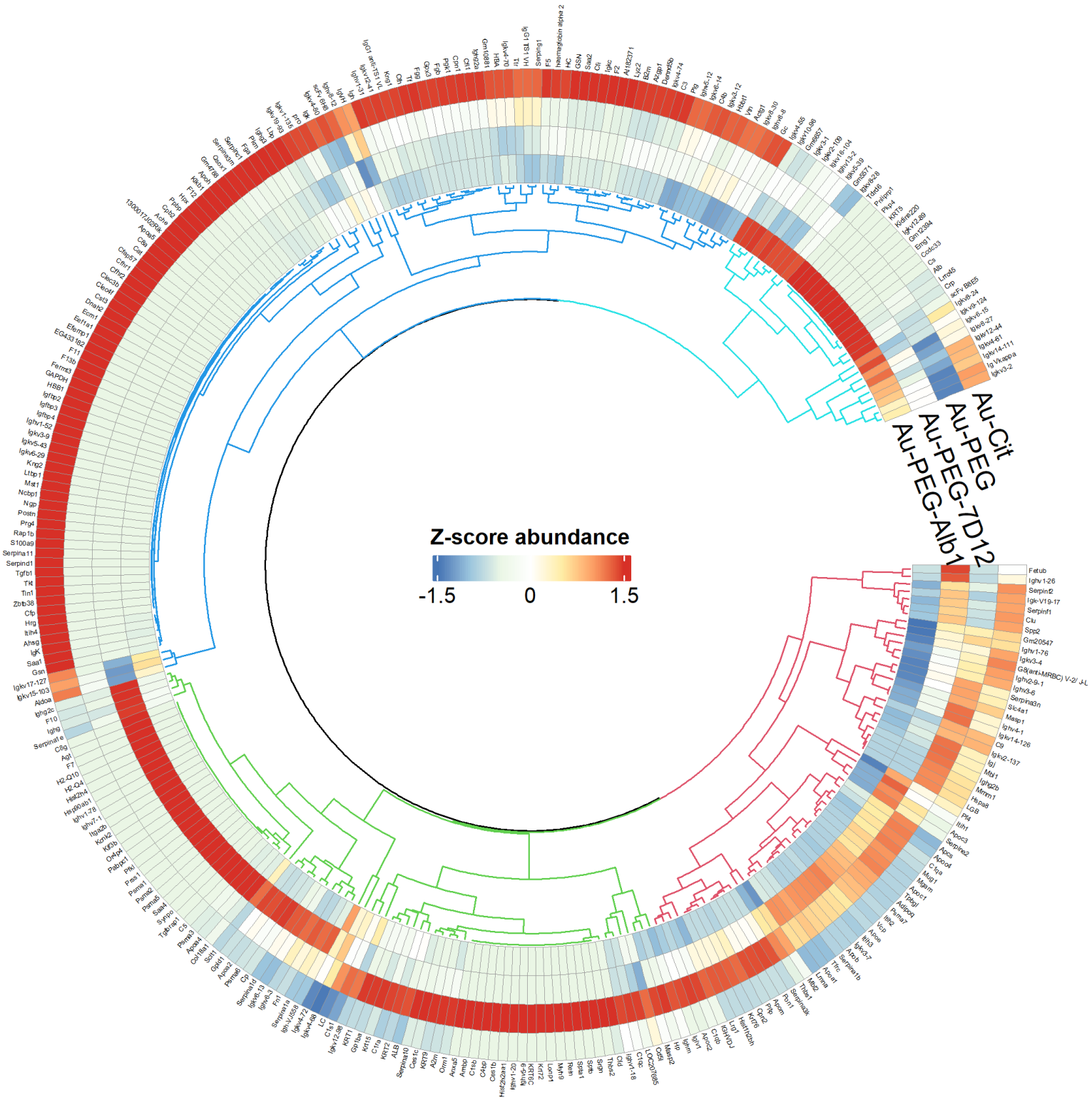

Figure S10. The heat map of all gene expression in each group. Analysis with MaxQuant.

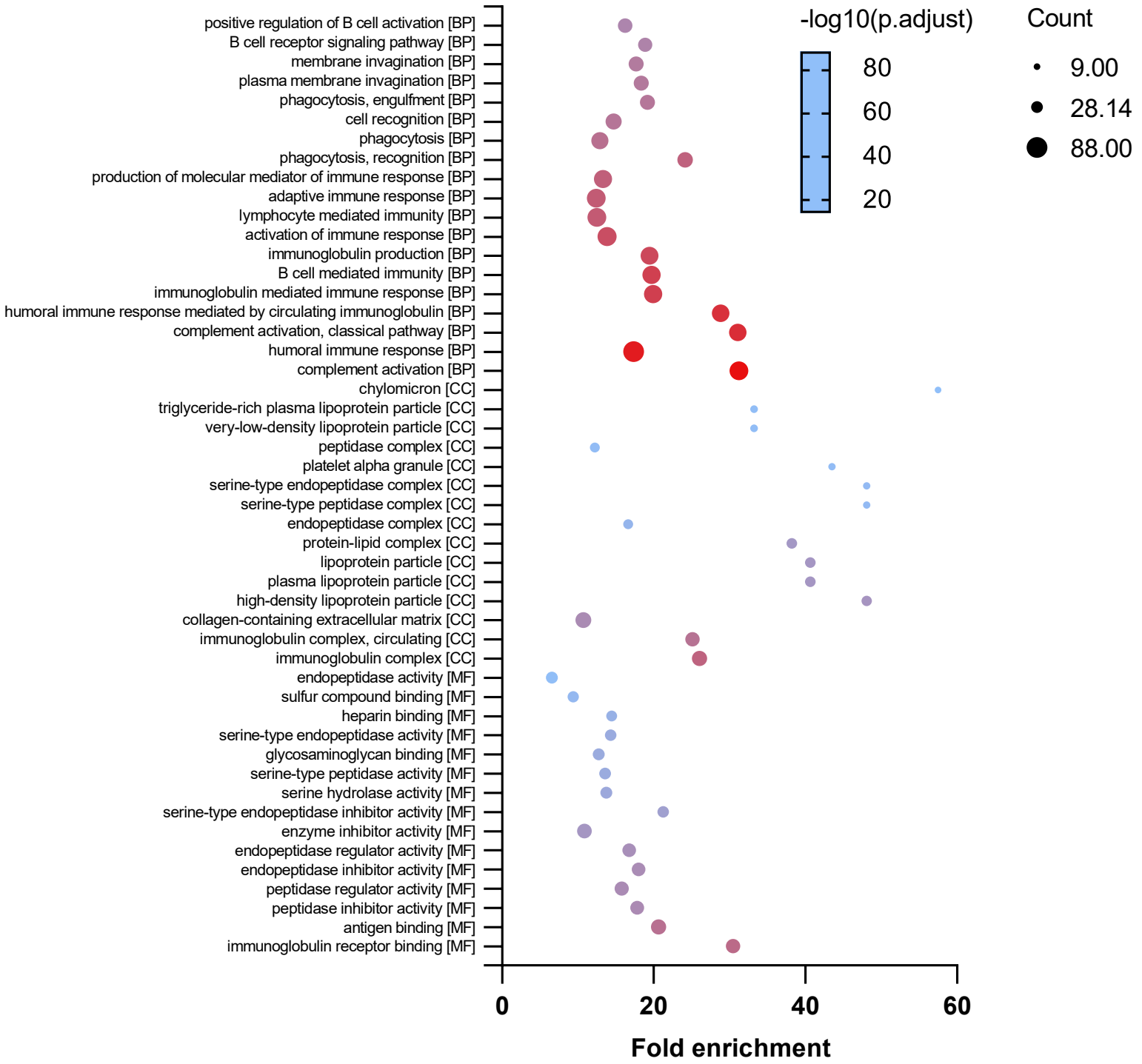

Figure S11. Gene ontology analysis of protein coronas. Significant enrichment analysis of corresponding pathways with KEGG pathway enrichment analysis.

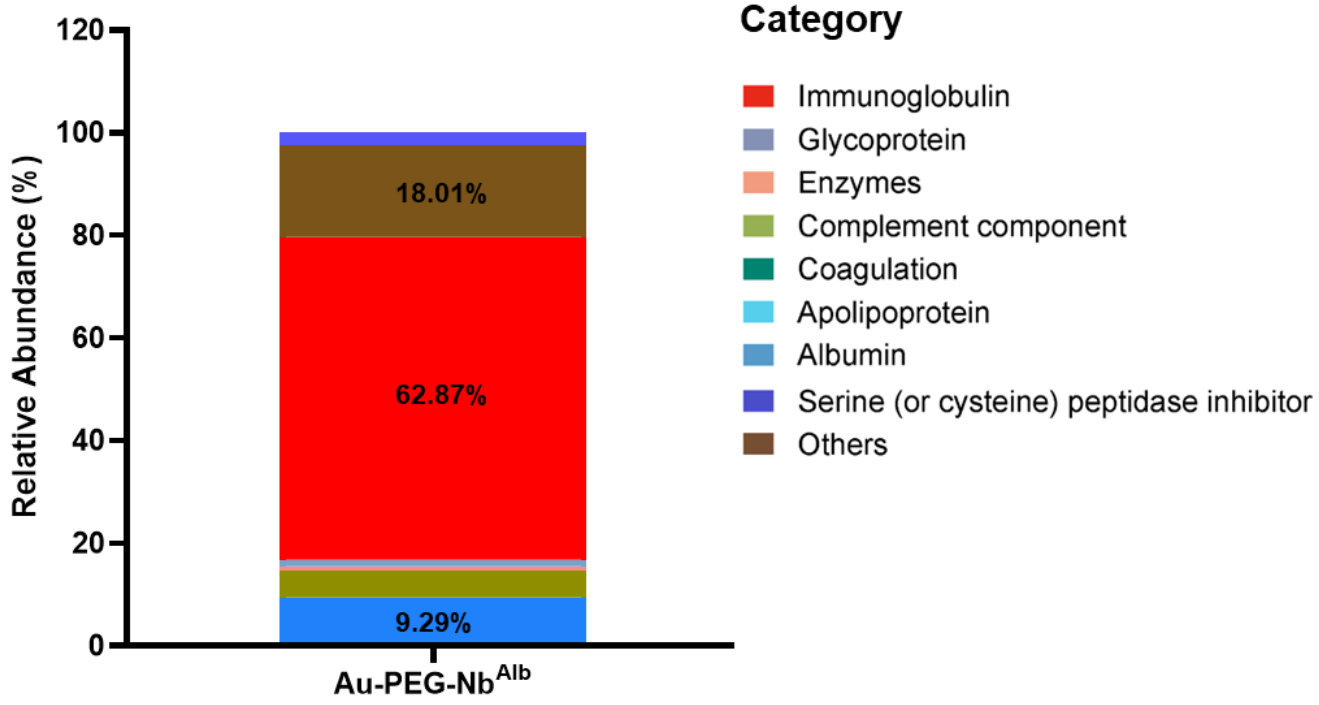

Figure S12. In addition to albumin, the relative abundance and classification of surface protein coronas in Au-PEG-Nb^{Alb}.

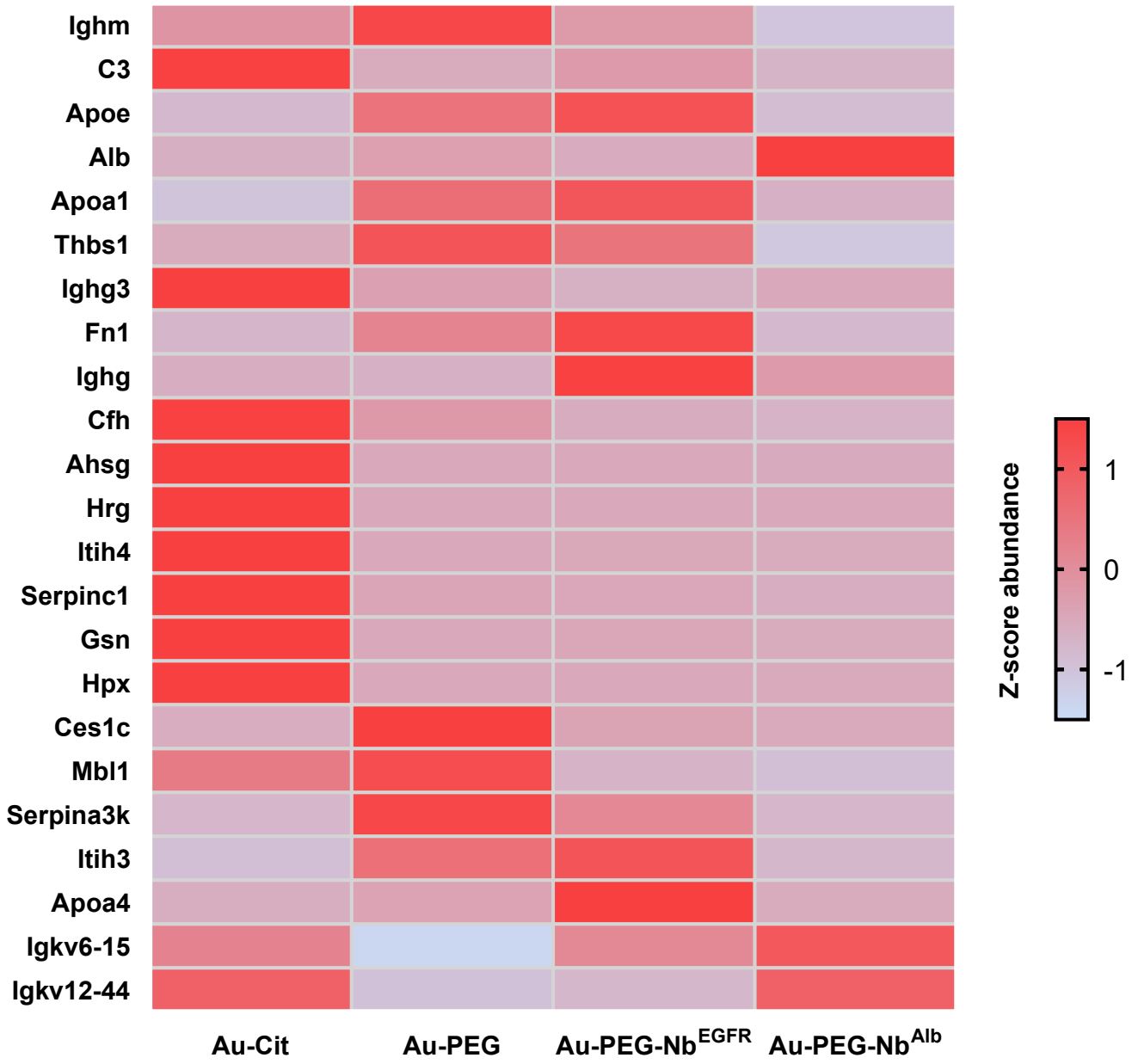

Figure S13. Analyzing results from MaxQuant using a heatmaps.

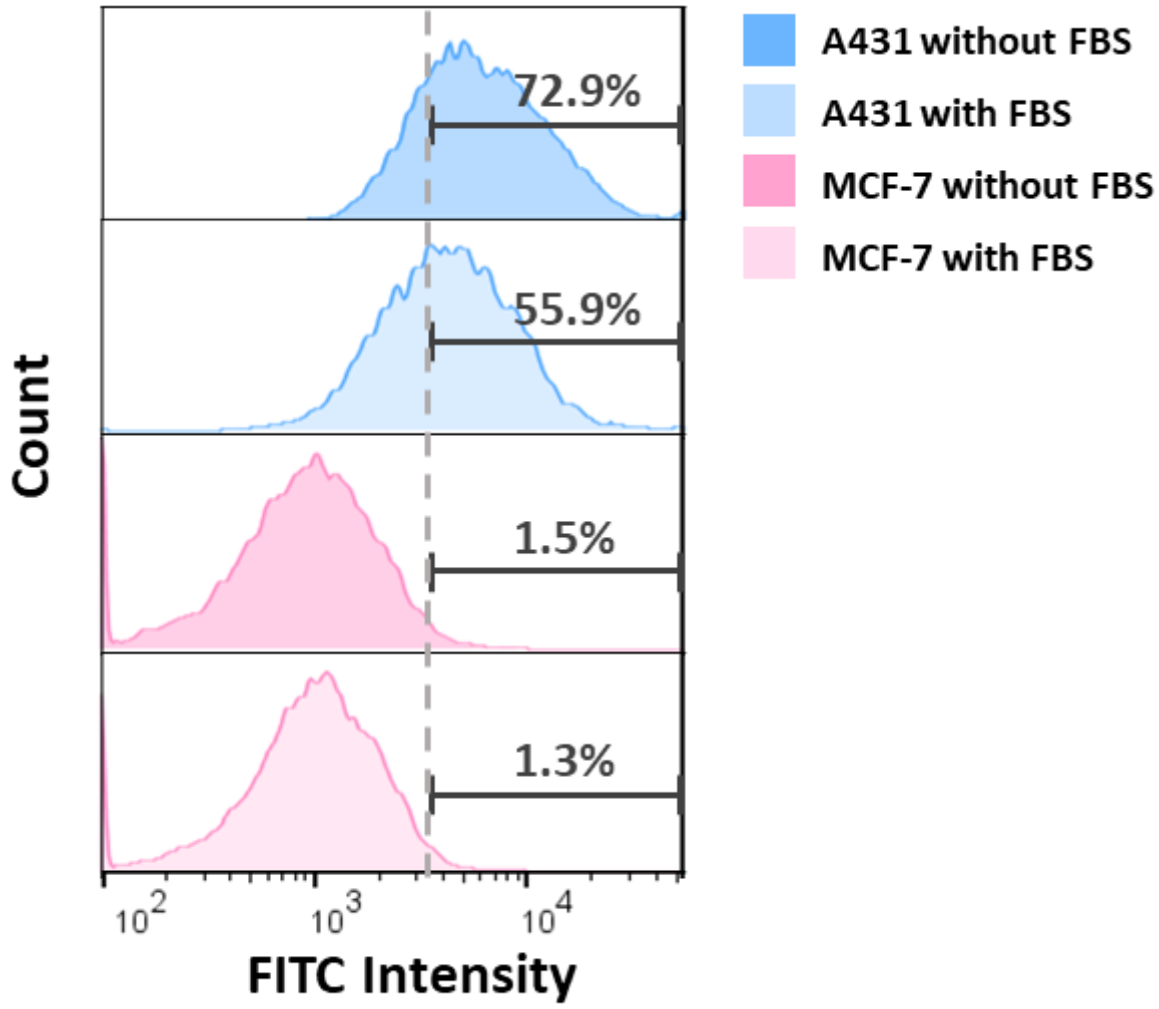

Figure S14. Flow cytometry analysis of cell internalization of Au-PEG-Nb^{EGFR} in A431 and MCF-7 cells. Cells were incubated with Au-PEG-Nb^{EGFR}-FITC (10 μM) in fresh medium with or without FBS for 4 h at 4°C.

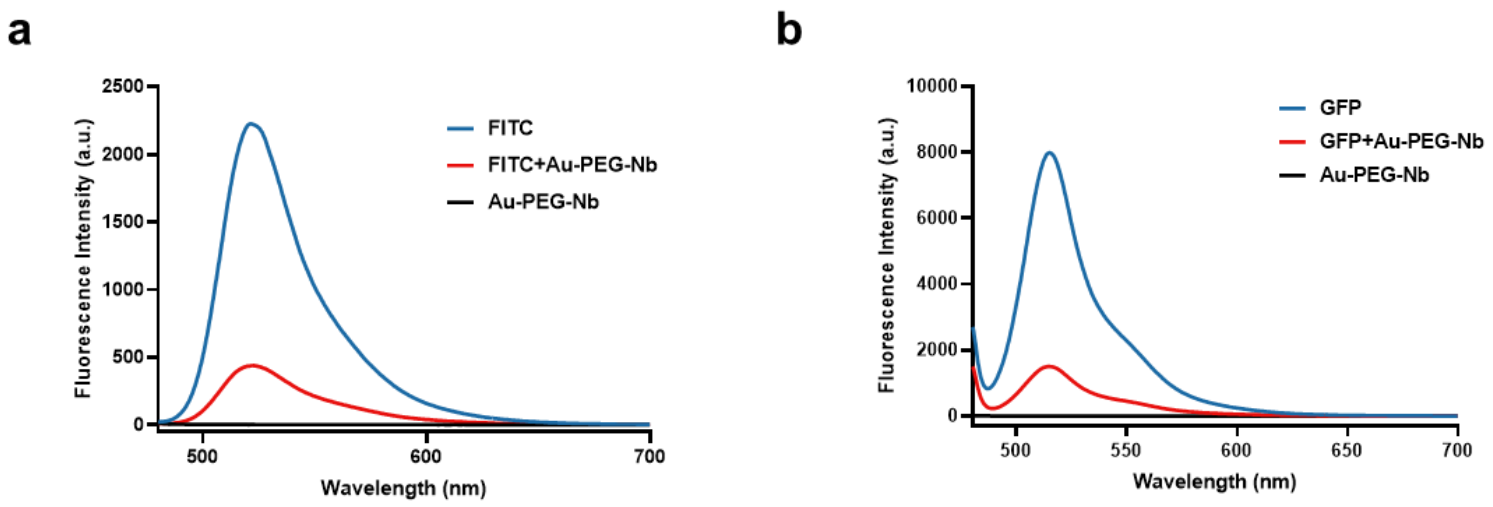

Figure S15. The ability of AuNPs to quench the fluorescence of FITC (a) and GFP (b).

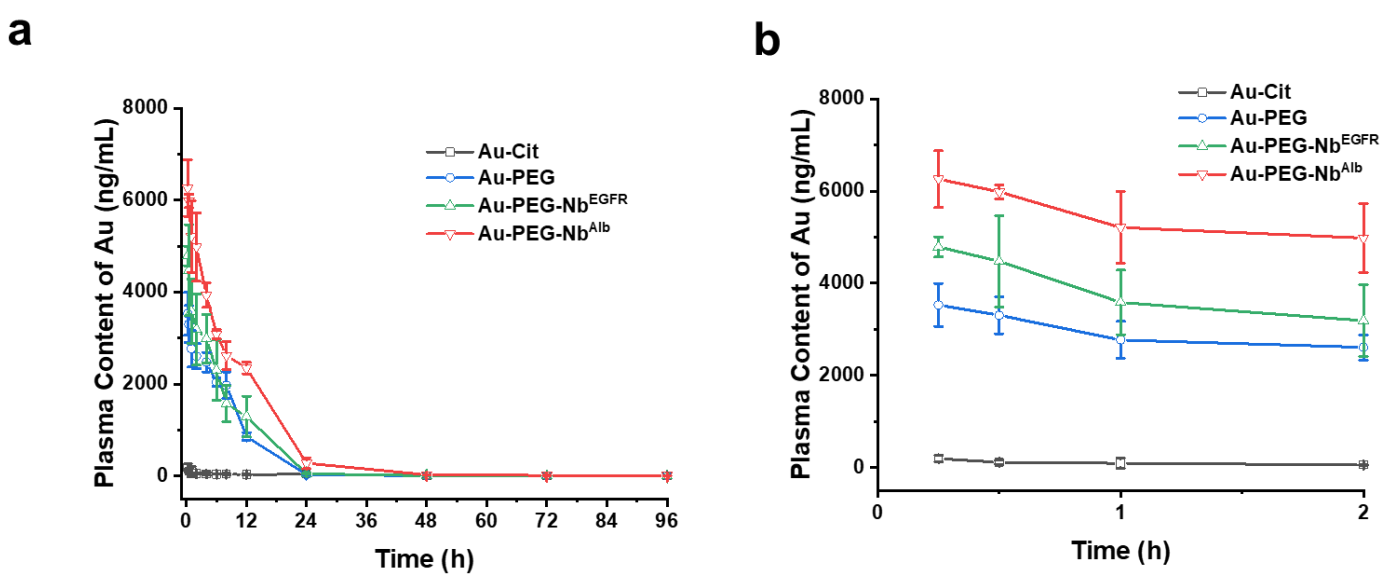

Figure S16. a. The metabolism of AuNPs with regulated protein corona. b. The metabolism of AuNPs in the first 2 h.