Abstract
Nanoparticles offer exciting new approaches for biomedicine ranging from drug delivery to cellular imaging. In the course of these applications, nanoparticles are exposed to a complex mixture of extracellular proteins that adsorb onto the surface of the nanoparticle. This “protein corona” dominates the interaction of nanoparticles with cells. We have investigated how proteins found in blood serum affect the cellular binding of protein-nanoparticle complexes. Using fluorescence microscopy, we find that the cellular binding of cationic nanoparticles is enhanced by the presence of serum proteins while the binding of anionic nanoparticles is inhibited. Competition assays confirm that these protein-nanoparticle complexes use distinct cellular receptors. Circular dichroism spectroscopy, fluorescence spectroscopy, and isothermal titration calorimetry show that the secondary structure of the adsorbed serum albumin is altered following adsorption on the surface of cationic nanoparticles. These structural changes redirect the albumin-nanoparticle complex to scavenger receptors. In comparison, the secondary structure of albumin is preserved following adsorption on anionic nanoparticles. The cellular binding trend is independent of nanoparticle composition: quantum dots, colloidal gold nanoparticles, and low-density lipoprotein particles all show the same behavior. This link between protein structure and cellular outcomes will provide a molecular basis for the design of nanoparticles for use in biomedical applications.