Lipid Coated Gold Nanoprisms as Sensors for Proteins-Lipid Interactions

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Purpose: Protein interactions with lipid membranes can determine much of the functionality of biomaterials and these interactions are likely size and shape dependent. As nanostructures become used more in biological systems, understanding how proteins interact with the surface is essential for the design of useful products. To this extent, we focused on the growing field of lipid coated nanostructures, a biologically compatible nanomaterial. The shape and coating were varied to test how different proteins bind to the nanostructures.

Methods: In this work, gold nanoprisms were synthesized using a seed-based method that gives rise to a mixture of nanospheres and nanoprisms. Nanoprisms were isolated using gel electrophoresis and sucrose gradient methods and characterized using transmission electron microscopy (TEM), localized surface Plasmon resonance (LSPR), and atomic force microscopy (AFM). Protein binding to the nanomaterials was tested using LSPR techniques, where a shift in the Plasmon resonance to lower energy indicated binding.

Results: Anisotropic gold nanoparticles coated with lipid bilayers leads to membranes with different curvatures. For example, the corners of nanoprisms (shown in Figure 1, inset) contain highly curved membranes while the plane sides have flat membranes. The anisotropy of the nanoprisms also leads to an interesting LSPR spectrum (Figure 1), with a major peak at 950 nm and a lesser peak at 525 nm. Anisotropic nanoparticles are biologically useful because they absorb near infrared light. In our work, we use the LSPR to study size and shape dependent interactions between protein and the nanoparticle membrane surface.

To test how proteins interact with curved lipid membranes, a peripheral membrane binding protein, C-reactive protein (CRP) and a pore forming viral protein, amphipathic α-helical (AH) peptide, were tested for their interaction with lipid-coated nanoprisms. CRP is a serum protein that binds phosphocholine in a calcium dependent fashion to begin a signal cascade that marks the lipid membrane of a dying cell, foreign particle, or LDL for removal by a complement immune response. CRP is upregulated 1000 fold during an acute infection and approximately 5 fold for chronic inflammation, as seen in patients with cardiovascular disease. Meanwhile, AH peptide interacts with lipid membranes by preferentially inserting in highly curved membranes. Recent work demonstrated that AH peptide selectively targets and destabilizes the lipid membranes with a diameter less than 75 nm. Since some enveloped viruses, such as HIV, are surrounded by highly curved lipid membrane, AH peptide has the potential to be utilized as an antiviral agent.

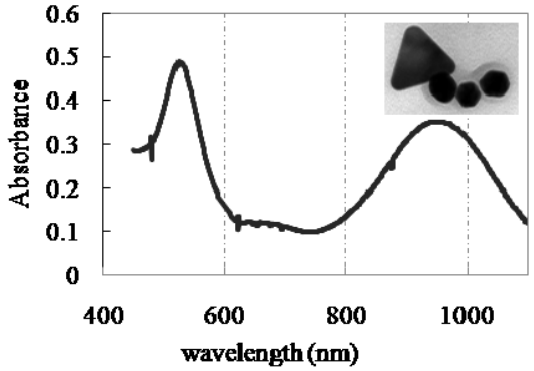

Figure 1. LSPR Spectrum of lipid coated gold nanoprisms in a mixture with gold nanospheres. The peak at 950 nm is due to the LSPR of the nanoprisms, whereas, the peak at 525 nm is due mostly to spheres. *Inset:* A TEM image of a gold nanoprism and gold nanoparticles (spheres) prior to purification. Image is approximately 175 nm wide.

Conclusions: In our work, novel nanomaterials are used to assay how AH peptide and CRP interact with lipid membranes and nanostructured materials in general. Our results demonstrate that gold nanoprisms are useful for detecting lipid-protein interactions and the LSPR signal can be used to assess protein binding to the surface. We have evidence that suggests that these proteins bind to smaller nanostructures with higher affinity than larger nanostructures. Using this assay and these materials, a broader study of protein-surface interactions can be made to determine if this is a general phenomenon or specific to these two proteins in the future.