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Electron Microscopy Investigations of Nanoparticles for Cancer Diagnostic Applications

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Abstract – There is increasing interest in the application of nanoparticles in medical research, particularly for early cancer detection and therapy. Our work concentrates on structural characterization. We are also developing and applying electron microscopy-based techniques to characterize the nanomaterial-biology interactions to determine binding between functionalized nanoparticles and cancer cells.

In recent years, researchers have started to explore the use of nanotechnology for early cancer detection. One way of achieving this will be to functionalize nanoparticles with antibodies that specifically bind to target analytes such as biomarkers on cancer cells. Using bio-sensing and detection platforms that recognize changes in sensor signals, (the presence of) the target analytes can be quantified via nanoparticle-biomarker conjugation. Accurate signal quantification not only relies on sensor design; the quality of the nanoparticles themselves is also paramount, as is the degree and specificity of binding.

This paper concerns structural characterization of Synthetic Anti-ferromagnetic (SAF) magnetic nanoparticles [1-3] and Composite Organic-Inorganic surface enhanced Raman (SER) scattering nanoparticles (COINs) [4-6] for in-vitro cancer diagnostic applications. We will also focus on the development and application of electron microscopy-based techniques to characterize the nanomaterialbiology interactions, to assess how, or indeed whether, nanoparticles are attaching to the cancer cells. We successfully determined the binding of CD54-functionalized COINs on the apicolateral portions of U937 leukemia cell lines using transmission electron microscopy (TEM), scanning electron microscopy (SEM) and scanning Auger microscopy techniques [7]. SEM imaging and SER spectroscopy correlation studies of different antibody-conjugated COINs attached onto different cancer cell lines show a direct correlation between the number of COINs binding to cells and the corresponding SER intensity [8]. Finally, TEM was used to locate intra-cellularly labeled COINs and to trace the phospho-stat6 signaling pathway in U937 leukemia cells, demonstrating that COINs can be used to detect intracellular phosphorylation signaling These experiments demonstrate the importance of electron microscopy for analyzing the events [9]. material-biology interface, for validating the attachment of nanoparticles on and in cells, and for its ability to provide complementary imaging and spectroscopic information to current magnetic and SERS bio-detection technologies.



Figure 1: (a) SEM backscattered electron image at 20kV showing the attachment of CD54-functionalized COINs (shown in box) onto the surface of a U937 leukemia cell. (b) Corresponding secondary electron image at 5kV. (c) Higher magnification secondary electron image at 5kV showing binding between COINs and the cell.

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