Abstract:

It is generally believed that adenocarcinoma of the esophagus originates in epithelial cells which have been transformed from squamous to columnar epithelial cells; a condition termed Barrett’s Esophagus (BE). Early detection of malignancy is crucial for designing an effective treatment and prevention method. The identification of which Barrett’s cells will become malignant is quite significant for improving patient survival rate. However, despite extensive study over the past several decades regarding the molecular pathogenesis of esophageal cancer, the selection of patients at risk remains largely unknown. Our long-term goal is to develop in vivo methods to characterize Barrett’s epithelial biology from cell surface markers. To achieve this goal, we sought initially to develop methods to detect epidermal growth factor receptors (EGFR) on the cell surface through surface enhanced Raman scattering (SERS). We specifically attempted to assess the effect of nanoparticle morphology (spherical vs. multi-branched) and the detection of Raman signal (i.e., finger print of the analyte). SERS is a sensitive, reproducible, vibrational spectroscopic method to analyze trace quantities of analytes. Gold nanoparticles (AuNPs) were employed to promote Raman signal enhancement due to their biocompatibility and optical properties. Two types of reporter dyes, specifically indocyanine (IR820 and IR792) and carbocyanine (DTTC and DTDC) were functionalized to the surface of multi-branched gold
nanoparticles, and stabilized with denatured BSA (dBSA), thus, forming the SERS tag. The SERS tags were then conjugated with anti-EGFR and then studied under Raman spectroscopy on the surface of normal esophageal cells and cancerous esophageal cells, Het-1A and CP-18821, respectively in order to detect differences in EGFR expression. Our findings demonstrate significant Raman signal enhancement as a function of the AuNP shape, i.e. multi-branched compared with spherical. It was observed that the Multi-branched gold nanoparticle (MBAuNP), had more SERS enhancement than that of spherical AuNP and that the monoclonal antibody (mAb) was successfully conjugated to the MBAuNP and the EGFR on the cell surface, Het-1A and CP-18821 was detected successfully. Future directions of this research should aim to confirm the in vitro results to in vivo study.