Detection and discrimination of rare cells from complex mixtures require high selectivity and throughput in order to get relevant results for clinical diagnostic. Current analytical methods are often drawn back by sources of artifacts that become apparent only when large numbers of cells are acquired. Moreover, the technique should be inexpensive, facile, and accessible to researchers without specialized training in silicon microfabrication, surface functionalization, and microdevice operation. Spectroscopic detection of rare cancer cells using biocompatible nanotags developed by chemisorption of fluorophores and/or Raman reporters on gold colloid was recently demonstrated as a method of high sensitivity and enough practicability.

In this regard we synthesized gold nanoparticles of various plasmonic responses (from visible to Near-IR), we conjugated the particles with fluorophores that overlap the plasmonic band of particles (fluorescein isothiocyanate, cresyl violet perchlorate) for maximum signal intensity and capped the nanoconjugates with polymer mPEG-SH for improved stability and biocompatibility. To attain specific recognition of non-adherent colon adenocarcinoma cells Colo320 (selected as a model cell line for circulating tumor cells), the fluorophore-particle conjugates were further functionalized with epithelial cell-specific antibodies. The nanotags were characterized by transmission electron microscopy, UV-Vis-NIR absorption spectroscopy, dynamic light scattering, zeta potential, fluorescence and/or surface enhanced Raman scattering (SERS) and found to be chemically stable and detectable inside cells down to nanomolar concentrations. For quantitative validation of the method, whole blood preparations were enriched with an increasing number of Colo320 tumor cells loaded with fluorophore-particle conjugates and also stained with a vital red fluorescent membrane marker (PKH26). Stained cells were quantified microscopically and by flow cytometry.

The presented results evidence the potential of spectroscopic-active nanotags to serve as ultra-sensitive imaging tools for rare cancer cell detection.

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