Surface-enhanced Raman Scattering for Rapid Diagnostics of Living Tumor Cells

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Metastasis is the most common cause of cancer-related death in patients with malignant tumors. Blood circulating tumor cells have been recognized as a possible way to contribute to development of metastases. The detection of the circulating tumor cells directly from the blood is also highly interesting for diagnosis and monitoring of the therapy. Advantage of using blood include that the sampling procedure is less invasive that taking biopsies. A challenge is the low number of tumor cells (typically few per 10^9 blood cells) [1]. We initiated a research program to discriminate tumor cells by Raman spectroscopy. Labels for surface enhanced Raman spectroscopy (SERS) can be applied to improve the sensitivity, specificity and throughput of a Raman based cell identification and Raman activated cell sorting. Compared with widely applied fluorescence dyes, SERS labels offer similar sensitivity with increased stability and multiplex capability due to narrow band widths.

A protocol was recently described to prepare “Multicore-SERS-Labels” (MSL) [2]. First step was controlled aggregation of 60 nm gold nanoparticles. The aggregated particles give higher enhancement factors at 785 nm excitation and show lower cytotoxicity. A monolayer of a reporter dye was adsorbed that provide a fingerprint like spectral signature. Polymer coating and a protective shell made of silica improve the stability of MSL. SERS spectra could be collected with few milliseconds exposure time at few milliwatt laser excitation intensity.

A marker for MCF7 cancer cells is EpCAM antigen. Therefore, MSL are conjugated with anti EpCAM antibodies for specific targeting cancer cells and for future capturing CTCs. The binding of functionalized MSL to cancer cells is demonstrated by dark field images and Raman imaging. As negative control cells without EpCAM antigen were subjected to the functionalized MSL. In the future, multiplex capability can be realized by MSL with further antibodies (e.g. against the cancer proteins EGFR or HER2 as antigens [3] and different SERS labels.

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