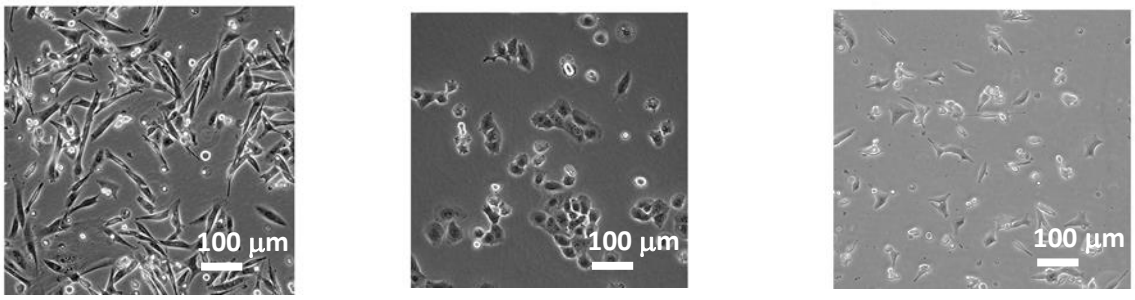
In the proposed project we will develop the new method for the detection and analysis of selected circulating tumor cells (CTC) of the breast, lung and prostate (Scheme 1) from the blood. The developed SERS-based diagnostic tool allows for the screening of the cancer disease, more precise determination and the enumeration of CTCs in the blood, and finally for eventual modification/change of the tumor treatment. Nowadays techniques used for CTCs enumeration are based mainly on the polymerase chain reaction. The proposed project will let the elaboration of the new diagnostic tool based on Raman effect for „liquid biopsy".

In the proposed project we intend to use both intrinsic (label-free) method for the detection of CTCs based on physical properties (different size membranes specially elaborated for CTCs and SERS analysis) and extrinsic format for the CTCs recognition based on their biological and chemical properties for multiplexing analysis of CTCs and for increasing sensitivity and specificity in detection of closely related CTCs cell lines.



1) MDA-MB-231 (ATCC® CRM-HTB-26™)
2) NCI-H1299 (ATCC® CRL-5803™)
3) VCaP (ATCC® CRL-2876™)

Scheme 1. Types of the selected tumor cell lines: breast carcinoma (1); lung (2); and prostate tumor cells (3).

Raman spectroscopy is a technique based on the study of oscillations of molecules and is characterized by a high selectivity. In Raman spectroscopy every molecules give molecular fingerprint specificity and information about the structure of the examined compound. However Raman process is relatively weak (approximately only one out of million photons are scattered in inelastic way). The intensity of the inherently weak Raman bands may increase by six orders of magnitude onto spots created in the gap between two nanoparticles, near sharp edges, tips. Based on that, new technique, so called surface-enhanced Raman spectroscopy (SERS) was established. In brief, surface-enhanced Raman scattering is an optical spectroscopy method with high sensitivity and chemical specificity. The phenomenon of SERS is explained by the combination of an electromagnetic mechanism and a chemical mechanism related to charge transfer between a substrate and an adsorbed molecule. The electromagnetic enhancement results from the amplification of light by excitation of surface plasmon resonance (SPR) of the substrate. This huge enhancement of Raman scattering (even single molecules can be observed) ensures that SERS spectroscopy is very effective for ultrasensitive bio-analysis. In our work we will use the SERS-active nanostructures based onto Ag and/or Ag-coated membranes to: (i) capture selected CTCs from blood samples (breast colorectal, prostate tumor cells (Table 1) and (ii) gain further insight into CTCs molecular structure, (iii) examine and understand the role of CTCs in cancer biology.

To summarize, the proposed project is linked to challenging and intensively developed, both in Europe and other countries, field of science and technology concerning novel "platform" for chemical and biological analysis with unprecedented routine levels of sensitivity, specificity and reproducibility. Development of novel technologies, including preparation of nanomaterials and functional materials in particular for applications in the health care and clinical diagnostics is considered by European Commission as one of the strategic direction. Our project is intimately linked to the fields mentioned above, as we are undertaking development of novel materials and methods for selective recognition of CTCs. Our work will offer both, basic understanding of processes linked with antigen–antibody interactions as well as understanding of the complex interactions between these molecules and plasmonic materials, and practical applications of the developed SERS-based diagnostic tool for enumeration of CTCs in the field of biomedical researches. These applications may be further developed into the practical prototypes.