Sensitive detection and visualization of cancer biomarkers using upconversion nanoparticles excited above 1000 nm

The main goal of the research project is the sensitive detection of prostate cancer biomarkers using upconverting nanoparticles (UCNPs) labels excited above 1000 nm. Additionally, the visualization of breast cancer cells will be carried out using immunocytochemistry (ICC).

The detection of cancer biomarkers is often done with immunoassays, of which the most common is the enzyme-linked immunosorbent assay (ELISA). The conventional ELISAs allow for measuring picomolar analytes concentrations, which is often insufficient for early cancer diagnosis. A method that enriches the analytes' limit of detection (LOD) is a single-molecule upconversion linked immunosorbent assay (ULISA). In the assay, luminescence labels are UCNPs that emit UV or visible light under near-infrared (NIR) excitation. The suitable labels should have a high emission intensity, easily distinguished in the biological background. In this project, the synthesis of core/shell $NaErF_4/NaYF_4$ and $NaTmF_4/NaYF_4$ is planned to meet project goals. The excitation wavelength will depend on the Ln^{3+} ions used: Tm^{3+} sensitizes NPs for 1208 nm and Er^{3+} for 1532 nm. Those wavelengths are located in the second (NIR-II) and third (NIR-III) biological windows, which possess higher contrast, deeper penetration depth, and the absence of autofluorescence. So far, no research group has attempted to change nanoparticles in ULISAs from commonly used 980 nm excited to those excited above 1000 nm.

To use UCNPs as cancer biomarkers, their surface should be modified appropriately and functionalized. The design of well-defined and stable labels is crucial for improving assay sensitivity. The UCNPs' surface conjugation with streptavidin (SA) by alkyne-PEG-neridronate will be used.

The analytes detection can be done using analog and digital readout. A conventional analog readout will determine the PSA concentration based on integrated luminescence intensity. Furthermore, the single sandwich immune complexes will be counted using a wide-field epiluminescence microscopy in the digital readout, which is much more sensitive than the analog one. These methods will allow us to verify the limit of PSA detection using obtained particles. Moreover, the SA-PEG-UCNPs will be used to label breast cancer biomarker HER2 in ICC. The microscope images and upconversion scans will confirm the labeling efficiency.

After heart disease, cancer is the most likely cause of death. The most frequently diagnosed type of cancer among men is prostate cancer, and among women, breast cancer. It is in the top five in terms of causing death from cancer worldwide. One of the critical prostate cancer biomarkers is PSA, the increased concentration of which determines incipient disease. Breast cancer is diagnosed in over 2 million women each year. Therefore, a quick diagnosis is crucial and makes it possible to start the patients' treatment at an early stage of the illness.

Using those labels and ULISA will improve the LOD of prostate-specific antigen (PSA) cancer biomarkers, allowing earlier stage cancer diagnosis. NIR-II and NIR-III excited NPs in the ULISAs will benefit the visualization of tumor cells.