A key function of the immune system is to distinguish normal cells in the body from foreign cells. When a foreign invader is detected, the entire immune system is alerted through chemical signals, just as a police station would radio police officers to alert them about a problem. When a virus attacks, we know the structure of the generated protein. And do we know what to look for when cancer attacks us? When a cancer invades our body the warning alert through chemical signals is less obvious. Some researchers say that cancer cells don't trigger an immune response because they are the body's own cells that have mutated-so those once-healthy cells no longer behave like normal cells. Because the immune system doesn't recognize the distinction, these cancer cells can continue to grow, divide and spread throughout the body. Our proposal put the research hypothesis: it is not true that cancer cells don't trigger an immune response. In cancers the chemical signals also exist, but we must use proper tools for detecting cellular signal transduction in cancers, distribution of these chemical signals in specific organelles of cells and tissues. Raman spectroscopy and imaging are an excellent tool that can not only provides biochemical profile of cells and tissues but also can monitor localization and biocomposition alterations in cancer as it progresses. Life and death decisions are made by cytochrome c? Life is oxydative phosphorylation (respiration), death is related to apoptosis. The dual-function of Cyt c comes from its capability to act as mitochondrial redox carrier that transfers electrons between the membrane-embedded complexes III and IV and to serve as a cytoplasmic apoptosis-triggering agent, activating the caspase cascade. We suggest that cytochrome c is a key protein in cancer development and is related to the entire immune system. There is evidence that Cytochrome c when is inappropriately located may behave as a damage-associated molecular patterns (DAMP) and induces an inflammatory response in the immune system. Recently we showed that at normal physiological conditions cyt c is located in the cell mitochondrium. Its release into cytoplasm triggers apoptosis. There are regulatory mechanisms for keeping balance between cytochrome c in the mitochondria and cytoplasm. We showed that a key role in this process is governed by interactions between cyt c and cardiolipine. At pathological conditions, cytochrome c is released to extracellular matrix, which is definitely an inappropriate place for it, because cytochrome c is recognized as DAMP molecule leading to inflammation. The release of cytochrome c into the interstitial space and the circulation is recognized by the immune cells through the same PRR receptors that recognize pathogen-associated molecular patterns leading to inflammation. Therefore, translocation of cytochrome c into the extracellular space provides the condition to act as an ideal DAMP. It has been reported that the critical element is the enzyme belonging to a broad family of cytochromes, CYP26A, which has been very well established to disrupt retinoic acid (RA) metabolism by promoting RA catabolism. It indicates that cytochromes are strongly coupled with retinoids. On the other hand, synthesis of retinoids is related to carotenoids. Briefly, β-carotene is cleaved by an enzyme of β-carotene 15,15'-oxygenase (CMOI) into two molecules of retinal (retinaldehyde). Retinal is catalyzed by the alcohol dehydrogenase (ADH) family to generate retinol, LRAT converts retinol into retinyl esters. Retinal catalyzed by ALDH1 or RALDH enzymes forms retinoic acid (RA) (transcriptionally active), which can metabolize by enzymes that belong to the cytochrome P450 (CYP) 26 family into more polar compounds, including 4-oxo retinoic acid, which are believed to be transcriptionally inactive. That is why we are interested in biocomposition alterations and biolocalization of the entire triangle: carotenoids-retinoids-cytochromes in cancers. Cancer is one of the most common and serious diseases in the European and world population and one of the main causes of morbidity and mortality, the conducted research provides innovative tools for improved (precise, objective and quick) diagnostics, response to drugs, design of new drugs based on the balance between the specific enzymes responsible for the synthesis or disruption of carotenoids, retinoids, cytochromes.

The research task is perfectly in line with the National Health Program 2016-2020. The project is in line with the strategic and operational objectives of the National Health Program 2016-2020, the National Program for Combating Cancer Diseases for 2016-2024, State Drug Policy 2018-2022. As a result, the project will contribute to understanding the mechanisms of metabolic reprogramming in cancer cells. Understanding the alterations of biocomposition and biolocalization as well as modifications of metabolic pathways will improve cancer Raman marker detection methods to cancer screening and early detection, and acceleration in immunotherapy and targeted drug treatments responses.