The goal of this Project is to *design and test novel, dual-mode electrochemical immuno-oligo-biosensors*, based on antibodies, aptamers, and molecular beacons, for the *investigation of the metastasis of human colorectal cancer cells* with different metastatic potential, as well as to *evaluate the utility of the survivin (Sur) mRNA expression as the target in cancer therapy,* based on the effects of *small-molecule survivin inhibitors.*

The following specific aims are designed to achieve the goal of this Project.

Aim 1: ***Design and testing of dual oligo-biosensors for the detection of EphA2 and ATP/Sur-mRNA utilizing electrochemical and nanogravimetric transduction techniques.***

Aim 2: ***Design and testing of dual immuno-oligo-biosensors responsive to EphA2 and Sur mRNA/protein for identification of metastatic cancer cells.***

Aim 3*: Utilization of dual immuno-oligo-biosensors for monitoring of cancer cells' migration and their invasion suppression by inhibition of Sur mRNA expression using small-molecule survivin inhibitors.*

Aim 4: ***To integrate the dual immuno-oligo-biosensors with a microfluidic chip to enable monitoring of a 3D metastatic tumor cell culture.***

Colorectal cancer (CRC) is the third most common malignancy and the second most deadly cancer type worldwide. The global number of new CRC cases (colon, rectal, anal) is predicted to reach 3.2 million in 2040, based on the projection of aging, population growth, and human development. Therefore, widespread early cancer diagnostics and novel cancer treatment strategies are highly sought after.

We will design different multiplex electrochemical biosensors, able to: (i) detect the proteins and mRNA, characteristic for cancer cells, (ii) distinguish between the metastatic and non-metastatic cancer cells by analyzing cargo contained in exosomes; and (iii) determine the expression of survivin mRNA/protein and EphA2 protein, carried by cancer cells and exosomes. The developed biosensing systems will enable us to monitor the decrease of the expression of survivin mRNA/protein and EphA2 protein in SW480 and LoVo cancer cells, achieved upon the treatment with small-molecule survivin (Sur) inhibitors (e.g., survivin antagonist S12; survivin inhibitors: YM155 and LLP-3) enabling to hinder the cancer propagation. This approach will enable us to gain deeper insights and improve understanding of cancer metastasis, elucidation of the survivin promotion of CRC metastasis mechanisms and prompt development of new techniques for cancer treatment using exosomes for the targeted anti-apoptotic drug delivery systems. The results obtained in this Project will allow us to extend the basic knowledge and will further enhance our ability for early cancer diagnosis and successful therapy.