Cancer incidents are significant public health and economic issue worldwide. The standard cancer treatment has changed over time from general chemotherapy, and radiotherapy to more personalized approaches considering, RNA and proteins expression, DNA mutations, tumor microenvironment, and immunologic response. Nevertheless, the majority of antitumor therapies are still only partially successful and have a lot of severe side effects. Therefore, novel, more efficient, and safe therapeutic approaches are urgently needed. Due to the substantial discoveries in the field of immunology and prominent progress in molecular biology methods, cancer immunotherapy has become a promising anti-cancer treatment.

Although the main role of the immune system is to protect the organism against pathogens, also cancer cells can be recognized and eradicated from the human body by specialized immune cells. Therefore the purpose of cancer immunotherapy is to enhance the patient's natural defences to fight the malignant cells, which try to escape from immune surveillance. The mechanisms that are involved in tumor eradication are based on tumor antigens presentation mainly by dendritic cells and activation of specific T cell clones capable of cancer cell killing. Thus the T lymphocytes were the first choice for genetic modification to express synthetic receptors that allow effective cancer recognition and elimination. In particular, T cells are isolated from patients' blood, expanded, genetically modified, and return to patients' bodies. The introduction of the sequence encoding chimeric antigen receptors (CAR) into the T cell genome allows to recognize and kill cancer cells, independently of commonly inefficient processes of antigen presentation and T cells activation in cancer. Though CAR-Ts have shown to be very effective in the treatment of B-cells derived leukemias still some limitations of these approaches diminished the effectiveness of CAR-T treatment in solid tumors. In particular, the infiltration of tumors by T cells is limited. Moreover, the immunosuppressive tumor microenvironment affects T cell function and leads to exhaustion and loss of antitumor potential. Interestingly, nowadays scientific data revealed that not only T cells ate engaged in cancer eradication. Also, macrophages and neutrophils are capable of cancer cell clearance. Neutrophils are the most abundant type of leukocytes in the blood and their main function is the eradication of microbes through a number of mechanisms, including phagocytosis, generation of reactive oxygen species, and production of extracellular traps. Since neutrophils and macrophages make up to 70% of tumor stroma cells it is valuable to genetically engineer these cells and use them as a cellular therapy. Therefore the purpose of this project is to modify neutrophils and macrophages to express CAR and evaluate their anti-tumor activity. Since the phenotype and function of neutrophils can be changed by a number of cytokines and factors produced by tumors the goals of this project include also choosing a treatment that will allow the maintenance of anti-tumor functions of neutrophils. The antitumor activity of CAR-expressing neutrophils (CAR-N) will be tested in in vitro and in vivo tumor models and the obtained results will help to understand better the mechanism behind the antitumor activity of neutrophils. In this project, we plan to generate a method of producing neutrophils that are effective in killing cancer cells as a new type of cellular therapy.