TUMOR-IMMUNE SYSTEM INTERACTIONS MODELING ON A SINGLE CELL LEVEL

Supervisor: Jacek Waniewski, Prof.
Co-supervisor: Jan Poleszczuk, PhD

Institute of Biocybernetics and Biomedical Engineering PAS

Department IV
Laboratory of Mathematical Modeling of Physiological Processes

Steady accumulation of genetic mutations by cancer cells leads to the creation of new tumor-specific antigens that can be recognized and attacked by the immune system. There are, however, several mechanisms in which cancer cells can become resistant to the immune system attack. Without a doubt, introducing immunotherapies based on checkpoint inhibitors which aim at overcoming those resistance mechanisms was a major breakthrough in the war against cancer. For some patients tumor responses to anti-PD-1/PD-L1 or anti-CTLA4 therapies are spectacular and last long after the therapy is withdrawn. Interestingly, disease regression can occur even after an initial phase of tumor growth during the therapy. However, despite spectacular successes, therapies based on checkpoint inhibitors still suffer from relatively low response rates and it is not completely clear what is the most prominent mechanism through which those immunotherapies achieve sometimes such an amazing efficacy. The goal of the proposed PhD project is to develop a detailed computational/mathematical model that describes tumor-immune system interactions on a single cell level and use its predictions to explain how immunotherapies, especially immune checkpoint inhibitors, lead to complete responses in some of the patients. An additional goal of the project would be to use developed framework to look for new therapeutic targets in the tumor-immune system axis. It is assumed that the developed model will be written as an agent-based model with cancer cells and various immune cells considered as a distinct type of agents. The model should be coupled with partial differential equations describing concentrations of various important substances in the tumor microenvironment. An example of tumor-immune system modelling using agent-based model can be found in the paper by Kather, Poleszczuk, et al. “In Silico Modeling of Immunotherapy and Stroma-Targeting Therapies in Human Colorectal Cancer” (access from http://cancerres.aacrjournals.org).