

Phenotypic heterogeneity in cancer chemotherapy

Principal Investigator: Bartłomiej Waclaw
Project Promoter: Institute of Physical Chemistry PAS, Warsaw, Poland
Project Partners: Hesso Farhan, University of Oslo/Medical University of Vienna

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In this project are investigated the differences in single-cell response of normal and cancer cells to chemotherapy, and how the response correlates with phenotypic, non-genetic heterogeneity prior to treatment. The project will help to better understand why chemotherapy fails, quantify the contribution of different mechanisms leading to resistance, and drive better, predictive mathematical models of cancer treatment.

It is envisaged to expose selected cell lines (glioblastoma, pancreatic cancer, lung cancer, normal fibroblasts) in vitro assay to a range of chemotherapeutic drugs, and imaged them using an automated microscope. Cells will be genetically modified to express fluorescent proteins to enable cell tracking and monitoring gene expression of selected proteins implicated in resistance. Images will be processed to extract features of interests (gene expression) and reconstruct phylogeny (cell relatedness).

By combining experimental data and mathematical modelling, it will be determinate the proportion of cells that survive treatment as a function of drug concentration and treatment duration, correlate survival with pre-treatment phenotype, and test simple models of evolutionary dynamics of in vitro chemotherapy.

Until now it was determined how the number of glioblastoma cancer cells change in time following exposure to the drug temozolomide and, also, generated genetically modified cell lines that will be used later in the project.