

Abstract for the general public

In spite of significant progress that has been made in diagnostic techniques and methods of treatment, cancer diseases are still a global public health problem, causing death of approximately 9 million people per year. Importantly, the main cause of cancer-related deaths is metastasis, that is, migration of cancer cells from the primary tumour to distant organs. Unfortunately, although new anticancer drugs are better tolerated and have fewer side effects, there is no strong evidence that they prolonging the life of cancer patients. Therefore, there is still an urgent need to find more efficacious drugs that not only inhibit the tumour growth but also have anti-metastatic potential.

The main aim of the herein project is to verify the hypothesis that new thiosemicarbazide-based human DNA topoisomerase II inhibitors have anticancer activity both in relation to proliferation and metastasis of cancer cells. The project will combine methods of computer-aided drug design with organic synthesis, molecular biology techniques and experiments on cell cultures and laboratory animals. The specific aims of the project are:

- to assess the effectiveness of the applied *in-silico* method to design thiosemicarbazide-based topoisomerase II inhibitors;
- to specify the molecular effect of 1,4-disubstituted thiosemicarbazide derivatives on cancer and normal cells;
- to select thiosemicarbazide-based lead compound efficient in three-dimensional cell culture systems and in a xenograft model of cancer, and having anti-metastatic activity.

We expect that implementation of the proposed research project will allow for comprehensive evaluation of anticancer potential of thiosemicarbazide-based derivatives and selection of the most promising anticancer drug-candidate. We also assume that due to the molecular mechanism of action of these compounds, they may be an element of combination therapy that increases the effectiveness of chemotherapy and radiotherapy.