One of the main problems in oncology is still drug resistance. Every year the number of publications concerning this issue increases but the number of patient does not decrease. One of the well-known causes of drug resistance in cancer is the mechanism associated with expression of genes coding for ABC family proteins and with their activity. These processes, however, are complex and we have not managed to identify a drug that would inhibit activity of those proteins and would appear efficient in clinics. Lately it was postulated that sensitivity of cancer drugs to therapy was correlated with telomerase. As suggested, this association might result from the fact that telomerase plays a pivotal role in genome stabilization. Undoubtedly, it is necessary to identify the mechanisms that cause resistance to drugs that are expected to provoke DNA damage in cancer cells that would lead to their death. We assume that the ability to modify drug resistance in cancer cells due to telomerase alteration followed by an increased sensitivity to drugs might appear an almost universal strategy in order to eliminate cancer cells with different proliferative potential (including cancer stem cells). So far we know, also from our previous studies, that decreased telomerase expression or inhibited activity of this protein was accompanied by an increased sensitivity to certain drugs (e.g. doxorubicin). Thus we come with the question – what is the mechanism of the sensitization.

So the aim of the study is to assess the correlation between telomerase modulation and drug resistance in an experimental model of cancer cells treated with telomerase inhibitors/modulators and cancer drugs. It is especially important since about the association between telomerase regulation, response to drugs, and drug resistance, except for our preliminary studies, we know not much yet. As the studied compounds we will use drugs with different mechanism of action: doxorubicin, cisplatin, actinomycin D, mitomycin C (DNA damage), paclitaxel (microtubule stabilization), verapamil (PgP inhibitor).

Performing all the planned experiments should enable identification of the network between telomerase regulation and drug resistance in cancer cells. We assume that this should result in an increased efficiency of cancer cells elimination, especially those most difficult to deal with i.e. drugs resistant. Thus, realization of the project may have a huge impact on the knowledge concerning the cancer metabolism which might contribute to alteration in our perception of cancer treatment strategy. We are convinced that our studies may constitute a crucial contribution to understanding the role of telomerase in cancer cells sensitization and DNA damage or repair in cancer cells treated with cancer drugs. Maybe this would even lead to the reversal of drug resistance.