The knowledge of the biology of cancer remains unsatisfactory. Due to the absence of this full knowledge, anticancer therapies are not completely effective. Personalized cancer therapy may allow for effective treatment and for minimizing its toxic effects to a minimum. One of the promising approaches for cancer treatment is personalized cancer therapy based on the synthetic lethality (SL) phenomenon. SL is defined as a combination of genetic mutations in two or more genes leading to cell death, while the mutation in each gene individually does not produce this effect. In this scheme, the cell loss of a gene involved in important cellular metabolic process, allowing for its survival is compensated by a second gene involved in the alternative pathway for this process. In the tumor cell, where the loss of one of these genes is very likely due to the magnitude of various types of rearrangements in the genome of the cell, its survival depends on the alternative gene. This second gene is a target for inhibitors. Disabling this alternative gene by the use of an inhibitor is a target for novel anticancer therapies. Tumors are often defected in DNA repair, suggesting that inhibition of the alternative DNA repair pathways may lead to eradicate them by SL effect. There are many DNA repair pathways, where one replaces another, e.g. homologous recombination repair (HRR) may be compensated by non-homologous end joining (NHEJ). Both of these types of repairs are the mechanisms repairing a DNA double-strand breaks (DSBs). In proliferating cells DSBs, the most lethal DNA lesions, are usually repaired by two major mechanisms, BRCA1/BRCA2-RAD51 (BRCA) dependent homologous recombination (HR) and DNA-PKcs-mediated non-homologous end-joining (D-NHEJ), whereas PARP1-dependent back-up NHEJ (B-NHEJ) serves as an alternate mechanism. HRR usually depends on BRCA, and RAD52-RAD51 serves as back-up and targeting RAD52 in cancer cells defected in main pathway, should kill them, by SL inducing. Also, PARP1 exerts an important impact on DSB repair rate, because this is a protein that binds to both single- and double-strand DNA breaks and later on modifies proteins involved in their repair. Because of SL, PARP1 inhibitors, like Olaparib, may be highly effective drugs in patients whose tumors have germline or somatic defects in DNA damage and repair genes. In the case of cancer cells without any defect in these repair systems it is possible to induce such defect by inhibition of histone deacetylases (HDAC), which reduces the activity of DSB repair key proteins, such as RAD51 or FANC2. The aim of the study project is to find the relationship between the cancer cells death caused by synthetic lethality induced by low molecular weight inhibitors targeting PARP1, RAD51 and HDAC proteins, and the molecular profile of DNA double strands breaks repair components. The research will be carried-out at 3 stages. At the first stage the key components of DSB repair, in tumors obtained from patients with brain, skin or pancreas cancer, as well as, cells derived from these tissues, will be identified. At Stage 2, cells possesses the same profile of DSB repair components as is in tissue, will be exposed to these inhibitors. At step 3, the resistant and sensitive cancer cells to inhibitors of DSB repair proteins, will be implanted to mice in order to verify the effectiveness of the elimination of cancer cells *in vivo*. It is expected that this study will increase the knowledge of cancer biology, based on DNA repair mechanisms, which is very incomplete to this day. Correlating of the DSB repair genes profiles, in different types of cancers, with response of cells to chemicals targeting the DNA repair proteins, causing SL-mediated death, may allow for better understanding mechanism of this process. Additionally, creation of the library of specific profiles of DSB repair components, associated with DNA repair-inhibiting effect of chemical compounds on the growth and development of various types of tumor cells, may allow for use of this model in the personalized therapy in the future, as a long-term goal.