Nowadays anti-tumor vaccines are in the focus of interest of numerous research groups. However, their efficacy largely depends on type of the used chemotherapy.

The main aim of the project is to elaborate a schedule of therapy exploiting multi-component chemo-immunotherapy, which will be used in two models of mouse tumors: colon cancer MC38 and melanoma B16.

Harnessing of the chemotherapeutics prior to application of cellular vaccines may enable renewal the immune cell reactivity to tumor antigens and can result in long-lasting delay of tumor growth not only by cytoreduction but also by elimination of particular subpopulation of the suppressor cells. As a chemotherapeutic agent, a nanoconjugate of methotrexate (MTX) hydroxyethyl starch (HES) which is a polysaccharide drug carrier will be used. Application of nanoconjugate of MTX and HES will provide prolonged effect in the body and reduce side effects compared to free MTX. Nanoconjugates MTX-HES enter into cells in a different way than free MTX – through folate receptor α, abundant on cancer cells, but this receptor is almost absent on normal cells. An action of the nanoconjugate will be complemented by immunotherapy based on genetically modified bone marrow derived dendritic cells (DCs) simultaneously producing IL-12 and IL-18 (alternatively IL-15) and stimulated with tumor antigens. As a temporary immunomodulator of local (tumor tissue) or systemic suppressive mechanisms the antibody against IL-10 receptor (IL-10R) will be applied.

There is increasing evidence that suppression of the immune response promoted by dysfunctional dendritic cells in the tumor microenvironment can be reversed by the use of dendritic cells generated and stimulated *ex vivo*. Therefore, attempts are being made to use different antigenic stimulators of DCs, for example, lysates of tumor cells. However, it is still an innovative approach a simultaneous introduction of cytokine genes to DCs, which may aid the maturation of the DCs present in host organism.

Results of analysis performed during this project will lead to estimate the efficacy of the applied chemo-immunotherapy containing cellular vaccines based on stimulated with TAg, transduced BM-DCs and MTX-HES nanoconjugate. and determination of phenotypic and functional diversity of cells present in the spleen and tumor tissues obtained from tumor-bearing mice. After the successful completion of the study, the elaborated scheme can be recommended to the clinical trials.

The project is a continuation of the research on the use of MTX and high molecular weight carriers in anti-cancer therapy and study focusing on the use of dendritic cell-based vaccine in mouse MC38 colorectal cancer.