CHARACTERISTICS OF TRAMP-C1 AND TRAMP-C2 SYNGENEIC METASTATIC MURINE PROSTATE CANCER MODELS WITH PARTICULAR EMPHASIS ON THE ROLE OF THE IMMUNE SYSTEM AND IL-33.

Mouse models of cancer are very important tools to investigate basic and preclinical research of new therapies. In relation to development of immunotherapy, models that mimic well the cancer immunology observed in the clinic are most wanted. The main aim of this study was to characterize TRAMP-C1 and TRAMP-C2 syngeneic metastatic murine prostate cancer models with particular emphasis on the role of the immune system.

In the *in vivo* studies, orthotopic inoculation of cancer cells was used. The orthotopic TRAMP-C2 model is characterized by a rapid growth of tumors, better blood flow in the tumor and increased metastases to the lymph nodes. Higher metastatic potential of TRAMP-C2 cell line is also observed after intravenous inoculation of cancer cells into the tail vein. The different metastatic potential of the TRAMP-C1 and TRAMP-C2 cell lines makes these models particularly useful in studies on prostate cancer metastasis.

During cancer progression in orthotopic models of TRAMP-C1 and TRAMP-C2, changes in the immune landscape were observed in the levels of inflammatory factors and the percentage of individual subpopulations of monocytes and lymphocytes. The analysis of subpopulations of lymphocytes in the blood and spleen suggests that the anti-cancer activity of the immune system is reprogrammed to pro-neoplastic activity with the development of cancer. Significantly larger changes were noted in the more aggressive model - TRAMP-C2, these results show that changes in the immune system may be of particular importance in prostate cancer metastasis.

Significant differences between TRAMP-C1 and TRAMP-C2 orthotopic models were observed in the level of IL-33, which plays an important role in immune homeostasis. In the tested models, higher serum concentrations of IL-33 correlated with higher tumor aggressiveness. Further *in vitro* studies showed that the effect induced by IL-33 may be concentration dependent.