Abstract

MHCI molecules are constitutively expressed in all nucleated cells and play a key role in antigen presentation to $CD8^+$ T lymphocytes. One of the tumor immune evasion strategies is MHCI expression downregulation. This leads to an impaired recognition of tumor antigens by $CD8^+$ T lymphocytes that are unable to start the immune response. Since the MHCI expression downregulation occurs in up to 90 % of some tumors it is neccesary to have a clinical relevant tumor model without a MHCI surface expression that would be used for testing of immunotherapeutic approaches.

This thesis describes a production of new model cell lines of TC-1 tumor cells with irreversibly downregulated MHCI. That was achieved by an inactivation of B2m, which is a part of MHCI, by gene editing using CRISR/Cas9. The B2m inactivation was confirmed by flow cytometry, western blot and sanger sequencing of single alleles. The inactivation slowed down the cell growth for both *in vitro* and *in vivo*. The cell metastatic activity was not affected. The tumors established by cells without the B2m expression are not sensitive to DNA vaccine against HPV16 E7 oncoprotein by a pBSC/PADRE.E7GGG vaccine. The main effector function against these tumors possess the $NK1.1^+$ cells. In a therapeutic vaccination experiment it was repeatedly achieved of tumor growth deceleration by combining DNA vaccination and ODN1826 adjuvans. DNA vaccination did not increase an antitumo effect when using the combination of ODN1826 and αTim-3.