Head and neck squamous cell carcionoma (HNSCC) is a malignancy that affects important anatomical structures of the upper digestive and respiratory systems such as: tongue, mouth, lips, larynx, throat and nasal cavity. Therefore, it can disrupt important life functions such as breathing, swallowing and speech, as well as cause negative psychological effects as a result of disease- and treatment-related deformations of visible parts of the body, what put it as an important clinical and social problem. The main risk factors associated with the development of this type of cancer are irritation of the mucous membranes of the mouth with carcinogenic substances contained in tobacco smoke and in high-percentage alcohol, as well as infection with human papillomavirus (HPV). In Poland, about 6,000 cases are diagnosed annually. Unfortunately, due to the non-specific symptoms, which are, among others, sore throat, sores in the mouth or hoarseness, patients are often diagnosed with locally advanced disease. Therefore, despite the combined therapy that includes surgery and radio- or chemotherapy, most patients have tumor recurrence or metastasis in other organs, which is the cause of high and unchanged over the years mortality: half of the patients diagnosed with cancer will not survive five years from the date of diagnosis. Therefore, understanding the basis of these processes is extremely important from potential therapies point of view.

The causes of metastasis and recurrence of cancer are not fully known. Scientific research indicates that the cancer is not homogeneous, it consists of cells with different properties. Some are more resistant to radiation and chemotherapy than others, which may result in their survival in the body after cancer therapy and the relapse of cancer. Due to the fact that the population of these cells is undifferentiated, extremely plastic and can give rise to all types of cells present in the cancer, which makes them similar to stem cells, it has been named as Cancer Stem Cells (CSC). Due to the involvement of CSCs in cancer relapses and their resistance to standard treatment, these cells are considered as future important potential targets for cancer therapy.

In the context of metastasis, current research suggests the involvement of the epithelial to mesenchymal transition (EMT) process in cancer progression. During the EMT process, the proteins responsible for adhesion between immobile epithelial cells disappear, resulting in gaining a mesenchymal phenotype and mobility by these cells. The transformation of non-motile epithelial cells into motile mesenchymal cells is considered one of the processes that enable metastasis of tumors.

The Bmi1 (B cell specific Moloney murine leukemia virus integration site 1) protein is one of the components of the Polycomb repression complex (PcG), which is involved in chromatin remodeling, that results in transcriptional silencing of specific regions of chromatin. In recent years, Bmi1 protein has been described as a potential marker of cancer stem cells in HNSCC. There are also studies showing its involvement in the EMT process, for example in breast cancer and melanoma. However, the role of Bmi1 protein in HNSCC is not well understood.

The aim of the project is to explain *in vivo* the role of Bmi1 protein in the process of tumorgenesis of head and neck cancers, as well as its *in vitro* function in cells derived from HNSCC. Created in our laboratory a mouse model with the Cre-Lox system enables to determine the role of Bmi1 protein in tumor formation. Due to the simultaneous presence of oncogenic K-ras and TGFβRII deletion, it is possible to induce the tumorigenesis process. Since Cre recombinase will be under the Bmi1 gene promoter, the tumorigenic process will only be induced in cells that express Bmi1 protein. In addition, the mice will contain the Rosa26Tomato reporter protein under the Bmi1 promoter, which will label cells expressing this gene and all their derivatives (these cells will be labeled in red). This system will determine whether Bmi1 positive cells are involved in the formation of cancers and what is their involvement in this process.

Additionally, we will perform a number of tests in *in vitro* cell cultures to verify the effects of knock-down and overexpression of Bmi1 protein on cell phenotype, as well as transcriptional changes will be investigated using RNAseq analysis. All the research proposed in the presented grant will contribute to a better understanding of the function of Bmi1 protein in HNSCC, which may lead to improvement of head and neck cancer therapy.