Head and neck squamous cell carcinoma (HNSCC) is the **sixth most common cancer worldwide**, representing over **half a million incidents every year**. Epidemiological studies have demonstrated that exposure to carcinogens such as tobacco and alcohol, as well as infection by oncogenic human papillomavirus 16 and 18, results in increased risk of HNSCC development. Currently, the treatment of choice for head and neck cancer is surgery, followed by postoperative chemo- and/or radiotherapy. **Despite advances in conventional methods, the 5-year mortality rate of patients with HNSCC has not improved**. With progress in technologies and molecular genetics, **there is a growing potential of gene therapy as a powerful tool for HNSCC treatment**. One of the promising therapeutic agents for this approach appear to be small molecules of micro RNA.

MicroRNAs (miRNAs) are a class of short non-coding RNAs that function as post-transcriptional regulators of genes expression. It was shown that miRNAs do not have an exclusively cell autonomous role but can be found in several body fluids such as tears, saliva, urine, breast milk and serum. It is believed that secreted miRNAs can participate in intercellular communication, affecting gene expression in adjacent and distant target cells.

There is now growing evidence that **dysregulation of miRNAs expression may participate in cancer progression**. In our preliminary studies **we identified 48 miRNAs** (25 down- and 23 upregulated), **which expression levels varied between tumor and healthy tissue specimens derived from HNSCC patients**. One of them was **hsa-miR-6510-3p**, which is nearly 6-**fold downregulated in tumor cells compared to healthy tissue**. Moreover, our preliminary studies on HNSCC cell lines (FaDu, H103) revealed that **miR-6510 decreases cell proliferation and migration in FaDu and H103 cells**.

The main aim of the project is **the identification and characterization of hsa-miR-6510-3p as a potential tumor suppressor in head and neck squamous cell carcinoma** (HNSCC). Authors of the project predict that **overexpression of miR-6510 inhibits proliferation of cancer cells, leads to cell cycle arrest and results in induction of cell death**. It is also believed, that **restoration of miR-6510 expression increases chemo- and radiosensitivity of HNSCC cells**. To verify this hypothesis, it is planned to realize the following specific objectives:

1. Establishing of the experimental model – HNSCC cell lines exhibiting miR-6510 up- or downregulation – using lentiviral vector or chemically modified antagomiRs respectively.
2. Evaluation of miR-6510 over-/underexpression effect on cell proliferation, motility and apoptosis *via* analysis of expression levels of genes involved in these processes.
3. Assessment of HNSCC cells chemo- and radiosensitivity after the miR-6510 down- and upregulation.

The study will be performed using the *in vitro* model of head and neck squamous cell carcinoma (two commercial cell lines: FaDu and H103; and at least two primary HNSCC cell lines derived from tumors of HNSCC patients.

Results of this project will be presented at international conferences as both oral and poster presentations. Due to the innovative nature of the project, the results will be published in international journals with high impact factor. This will allow to extend the current knowledge about the **role of micro RNA hsa-miR-6510-3p in the pathogenesis of head and neck squamous cell carcinoma and the possibility of its applying in the gene therapy of these malignancies**.