The head and neck squamous cell carcinoma (HNSCC) is one of the most common cancers worldwide with roughly 890 000 new cases in 2018 only. Moreover, the incidence rate is still alarmingly rising, especially in the group of young, non-smoking men in developed countries who underwent human papillomavirus infection (HPV). Major risk factors for developing HNSCC are excessive, long-term alcohol and/or tobacco consumption, environmental carcinogens, and HPV infection. Interestingly, individuals not exposed to HPV have worse treatment response and thus the prognosis in comparison to patients after infection. However, there is still an urgent need for education and vaccination programs in this particular group of younger people. HNSCC develop tumours in the mainly in the larynx, oral cavity, and pharynx. This group of malignancies is known for its heterogeneous character which make the standard methods of HNSCC therapy, such as chemo- and radiotherapy, surgical resection, or systemic treatment with, e.g. carboplatin, cetuximab, and cisplatin bring unsatisfactory results. It has been proven that even aggressive multimodal treatment leads to subsequent relapse in nearly 50% of patients. The high mortality rate is the main motivation behind the search for molecules that could serve as future therapeutic targets or drugs themselves. However, personalized treatment is not always an answer to the common problem of late detection of already advanced disease. That is why it is extremely important to find biomarkers of the early stage of HNSCC that could be used as a diagnostic screening panel.

In recent years non-coding RNAs (ncRNAs) have gained a lot of interest as a promising source of knowledge about human and cancer biology, mechanism of disease progression, and therapy response. Additionally, it has been proven that a multitude of them could serve in the future as diagnostic biomarkers specific for a particular type, or even stage, of a tumor. MicroRNAs (miRNAs) are molecules with the ability to regulate gene expression. Over the years, many researchers have proven miRNAs involvement in a lot of cellular processes pivotal for cancer development. Moreover, many of them were characterized as inhibiting cancer - suppressors or promoting tumour growth - oncogenes in different malignancies, including HNSC. Chosen for this study miRNA - miR-27b-5p - is aberrantly expressed in a multitude of cancers. This miRNA is also already known for its association with tumour growth, metastasis, along with impact on patients treatment and prognosis. The miR-27b-5p was selected by us based on previous experiments on its interaction with long non-coding RNA (lncRNA) LINC00052, which showed the positive effect of the simultaneous high expression of this miRNA and low expression of lincRNA on the overall (OS) and relapse-free survival (RFS) of patients with HNSCC. Our interest in non-coding RNAs stems from their known broad involvement in the complex web of interactions and signaling pathways taking place in both healthy and cancer cells. In previous years, our team managed to prove the important role of ncRNA molecules such as let-7d, miR-18a, miR-205, ZFAS1, and EGOT lncRNA, as well as LINC00052 in HNSCC biology. We have also repeatedly emphasized the potential of the above circulating ncRNAs as predictive and prognostic biomarkers, which determination using the liquid biopsy technique may revolutionize the diagnosis of this group of cancers.

The aim of the project is to investigate the potential of miR-27b-5p as a biomarker in HNSCC. The above study will elaborate on this miRNAs expression level changes depending on type of the tissue (healthy, tumour), localization of the tumour (the larynx, oral cavity, pharynx), and HPV status (positive, negative), but also will elucidate how standard cancer treatment affect the amount of said miRNA and molecules that miR-27b-5p interacts with (targets), whose function will be analyzed in cell line models through reporter system. Our work will be based on paired cancer and matched adjacent normal samples collected in Greater Poland Cancer Center (GPCC) Poznan by our team with assigned clinical-pathological data, as well as, on relevant cell lines (used by us before and available in our laboratory) and will include not only the assessment of the expression level of miR-27b-5p, but also functional analysis of its targets which were previously selected through bioinformatic search of the TCGA as well as GEO database. The effect of irradiation and chemotherapy on the levels of this miRNA and its targets in cell lines will be tested by assays checking their viability, mobility, ability to divide and grow after exposure to selected factors. All of the obtained data will be analyzed and compared to the TCGA and GEO database, creating a complete picture of the molecules' potential as a future HNSCC biomarker.

We believe that a properly conducted functional analysis of the miR-27b-5p targets may contribute to the specification of the HNSCC dedicated panel of biomarkers. We are convinced that defining the role of the above miRNA will allow us to better understand and characterize the HNSCC, and to answer the question of whether miR-27b-5p will be able to become a biomarker of detection, treatment response, or disease stage in the future. Our work can contribute to faster diagnosis and personalized treatment for patients with HNSCC.