ABSTRACT

Head and neck cancers represent a group of tumors with two different etiologies. The first type is associated with the viral HPV infection, the second one is virus-independent and it is associated with smoking and alcohol consumption as two main risk factors. Numerous studies show that HPV-positive tumors are more frequent in younger patients, as well as that the prognosis and overall survival of these patients is remarkably better. Therefore, the modification of the treatment is considered. For this, however, specific, sensitive and clinically relevant biomarkers for accurate identification of tumor etiology is needed. Suitable candidates for such biomarkers are miRNAs, small non-coding regulatory molecules stable in archived samples, that have been shown as differentially expressed in human cancers and the expression pattern seems specific for tumors of different origin.

The submitted thesis focuses on miRNA profiling in HPV-positive and HPV-negative tonsillar tumors and cervical carcinomas with the aim to find out the differences between regulation of important carcinogenetic pathways of tumors of viral and non-viral etiology. Our data have shown very large heterogeneity of the miRNA expression profiles of these tumors. Despite the well characterized and uniform samples collection, we have found very small overlap of the HPV-specific miRNAs in comparison to both our model system and to other studies. Therefore, we focused on the reasons for such heterogeneity, this study has shown the importance of the homogeneity of analyzed samples and standardization of the type of clinical material and normalization approach for data analyses.

Overall, the submitted thesis presents our results from miRNA research of HPV-related cancers. During the research, several important observations were made which allow for the improvement of the next experiments. Finally, the HPV-core miRNAs were identified and will be evaluated in a following project in a set of HPV-related and non-related samples from malignant tissues of other anatomical locations. These selected miRNAs will be then analyzed functionally.