Popular summary (OPUS): Functional analysis of novel oncomiR candidates in classical Hodgkin lymphoma

Research project objectives/Research hypothesis

Classical Hodgkin lymphoma (cHL) is one of the most frequent lymphoma type especially in young adults. This disease is characterized by a yet not fully understood interplay of genetic and epigenetic deregulation. In our recent project we have identified a group of deregulated miRNAs, short RNAs of regulatory function and important members of the epigenetic cellular machinery, in cHL. Within this group we found a novel group of overexpressed miRNAs not reported in the literature in relation to cHL pathogenesis and expressed at significantly lower levels in any of the controls analyzed. Intrigued by this finding we hypothesize that these potential oncomiRs have an important, yet unknown function in the pathogenesis of cHL. Therefore, the aim of this proposal is to identify the biological function of these miRNAs in the pathogenesis of cHL.

To decipher the function of these miRNAs in the first part of the project we will silence the expression of these miRNA in selected cHL cell lines and perform downstream functional assays to observe changes in cell viability and survival. MiRNAs showing the strongest effect will be further analyzed in a procedure called AGO2-RIP-seq combined with global proteomic profiling (LC-MS/MS). The set of target mRNAs and the respective proteins regulated by the analyzed miRNA represents the targetome of the studied miRNA. By using bioinformatical analysis of the targetome we will decipher the biological function of the miRNAs of interest.

In the last step we will experimentally validate selected miRNA-mRNA interactions using reporter assay.

Expected impact of the research project on the development of science

The role of the miRNAs selected for analysis in this proposal in the pathogenesis of cHL is completely unknown. We expect to decipher their function and to demonstrate the important role of some of these candidate miRNAs in cHL. Therewith, this project will bring us closer to understand the complex (epi)genetic deregulation behind this disease. The results of these study may also provide novel therapeutic targets for cHL.