Abstract:

Oncogenic microRNAs (miRNAs) are small RNA molecules that inhibit post-translational regulatory mechanisms at the epigenetic level. miRNAs are often deregulated in malignancies and due to their stability are detectable in non-cellular fractions of peripheral blood. In our laboratory, we have performed several studies that have investigated and utilized miRNAs as biomarkers for various hematological tumors (e.g., chronic lymphocytic leukemia, Hodgkin`s lymphoma) and solid tumors (e.g., breast cancer). The aim of these studies was to find the association of miRNAs with pathophysiological and clinical aspects of each disease. Here, we confirmed the importance of particular miRNA or its complex during disease monitoring. Combining clinical, molecular biological and statistical analyses, we were able to find miRNA sets that fulfilled not only a diagnostic role but also a prognostic role beyond expectations.

The main focus of this thesis is on the investigation of microRNAs in the diagnosis of a hematological malignancy - primary cutaneous T-cell lymphoma (CTCL). Tumor specificity of some miRNAs has been demonstrated. Their aberrant expression in tissue samples of CTCL patients obtained from skin biopsies, correctly distinguished malignant disease from control samples of benign skin lesions. Here, we asked whether these miRNAs could be used as plasma biomarkers for clinical monitoring of CTCL. From repeated peripheral blood samples from CTCL patients and controls with benign skin disease, we detected miRNAs using specifically activated RT-PCR. As a result, was established a model based on upregulation of miR-155 and downregulation of miR-203 and miR-205 with 100% specificity and 94% sensitivity from plasma samples of CTCL patients. The model of 3 miRNAs in consecutive samples was consistent with the clinical status of patients, with therapeutic response, and with change in tumor size. Quantification of selected microRNAs in plasma is a specific method to evaluate CTCL, which is a valuable tool for diagnosing CTCL and monitoring response to therapy.

Keywords: microRNA; mycosis fungoides; Sézary syndrome; cutaneous T-cell lymphomas (CTCL); atopic dermatitis.