Abstract

Deregulation of gene expression caused by genetic or epigenetic changes plays an important role in pathogenesis of cancer. The thesis is a commented collection of ten publications dealing with the molecular biology of tumours. The author has significantly contributed to all of them. All the articles contained in the thesis are linked to the topic of assessment of molecules involved in gene expression regulation (microRNAs) or DNA alterations that affect gene expression (promoter methylation, presence of a fusion gene). MicroRNAs are short single-stranded RNA molecules involved in posttranscriptional regulation of gene expression by triggering mRNA degradation or inhibiting translation. It is a basic mechanism with an impact on all cellular processes including the pathogenesis of various diseases. MicroRNAs can either act as oncogenes by decreasing the expression of tumour-suppressor genes or as tumour-suppressor genes by decreasing the expression of oncogenes. However, the network of microRNA – RNA interactions is much more complex. Our published results that are part of this thesis are focused on colorectal carcinoma (CRC), prostate cancer, head and neck squamous cell carcinoma (HNSCC), gastric cancer and non-small cell lung cancer (NSCLC). In patients with CRC, we demonstrated the prognostic significance of miR-21. In prostate cancer tissue, we have described higher miR-20a expression in less differentiated tumours with higher Gleason score and showed that the presence of the TMPRSS2-ERG fusion gene is related to worse prognosis. A new finding in HNSCC was a relationship between the miR-34a expression and p16-positivity as an HPV infection marker. We found microRNAs (miR-150, miR-224 and miR-342) with prognostic significance in patients with advanced gatric cancer. In the group of NSCLC patients with advanced squamous cell carcinoma treated with palliative chemotherapy, we found a relationship of miR-34a, miR-224 and miR-342 to overall survival, but also showed that the high level of one particular microRNA may under certain circumstances be associated with an unfavourable prognosis, under other conditions, the patient's outcome is good. Results on the basis of the microRNA expression estimation in biological material (native tumour tissue, formalin fixed paraffin embedded tissue, blood plasma) indicate that these regulatory molecules can reflect the clinico-pathological features of the tumours and could become clinically applicable biomarkers.