Summary

The incidence and mortality of gastrointestinal cancers are at a level that represents a serious problem. These tumours have non-specific clinical symptoms, which often results in late diagnosis. In recent years, there have been significant advances in the identification and monitoring of molecular markers of tumour changes in the diagnosis, prognosis and treatment of these diseases. However, clinical oncology still faces a shortage of such biomarkers. The aim of this study was to find new biomarkers that correlate especially with prognostic indicators and predictors of treatment response or chemoresistance in gastrointestinal tract cancers.

This thesis is based on 5 studies addressing ductal adenocarcinoma of the pancreas, colorectal cancer and hepatocellular carcinoma using IHC and molecular methods. All studies were performed using archival formalin-fixed paraffin-embedded samples. The main results include immunohistochemical evidence of protein expression of MRP2, SLC22A3 and SUR1/*ABCC8* transporters and its significant association with the prognosis of pancreatic adenocarcinoma. Patients without SLC22A3 protein expression in the apical membrane were found to have significantly shorter disease-free and overall survival. We found longer disease-free survival in patients with positive membrane expression of both MRP2 and SLC22A3, and shorter overall survival in the combination of positive MRP2 and negative SLC22A3 expression. Patients with moderate or high expression of SUR1/*ABCC8* in the cytoplasm had a 3.5-fold higher risk of disease progression compared to patients with low expression. Another study showed that the presence of T and B lymphocytes in the inner invasive margin of hepatocellular carcinoma after resection was associated with a favourable prognosis for the patients. In the same disease, the presence of mutations in *CTNNB1*, *TERT* polymorphism and CD8+ lymphocyte density were significantly associated with longer time to recurrence. In the last submitted study, we show the importance of exome sequencing for characterizing the molecular profile of metastatic colorectal cancer. We confirmed the high frequency of somatic variants in *APC*, *TP53* and *KRAS* genes in paired samples of primary lesions and synchronous liver metastases and the similarity of mutational profiles in samples from both tumour types.

In the framework of this PhD thesis, several new approaches for the use of archival samples of gastrointestinal cancer tissues have been proposed and a number of new biomarkers have been identified to determine the prognosis of patients. Further independent studies in larger patient cohorts are needed to confirm our findings and to introduce these biomarkers into clinical practice.