Summary

Progress in proteomic technology has been enormous during last few years. Clinical proteomics provides scientists and clinicians with better understanding of cancer biology, and in the future it can be a powerful tool to develope new diagnostic strategies.

This doctoral dissertation consists of a series of five publications, where comprehensive method of large scale proteomic analysis of archival formalin fixed and paraffin embedded colorectal tissues using mass spectrometry was described. Main goal of this research was to analyze the changes in the protein composition associated with adjacent normal mucosa- colonic adenoma-colorectal cancer sequence model. Using only minute amounts of microdissected material, over 10 000 proteins were identified. Drastic proteomic remodeling was observed between healthy and neoplastic epithelial cells, including extensive alterations in cell surface and nuclear proteomes. Additionally, the changes in energy metabolism, plasma membrane transport, DNA replication and transcription was described.

To my knowledge, this is the greatest proteome coverage achieved in the studies of clinical material thus this doctoral dissertation established a quantitative protein repository of colorectal cancer. Another important implication of this research is that proteins alteration identified in large scale analysis covers previously identyfied potential biomarkers and may be validated using traditional immunohistochemical methods.

8