

During the last years we have observed a rapid development of molecular genetic diagnostics (DNA diagnostics). New methods and technologies are rapidly being introduced and the spectrum of genetic services is gradually extended. Since germline genetic tests might have lifelong influence health and quality of patient's life, all efforts should aim at improvement of the overall quality of provided diagnostic services. An increasing number of laboratories replace their "in-house" developed techniques by the commercial diagnostic assays, but they often modify manufacturer's instructions. Therefore, it is necessary to validate and verify all methods and techniques before their implementation into routine DNA diagnostics.

In this thesis I have focused on evaluation and application of High Resolution Melting (HRM) in clinical diagnostic practice based on its comprehensive validation, according to the major international quality assurance standard ISO 15189. On the model of selected genes (BRCA1, MTHFR, CFTR) we have confirmed the high utility of HRM for mutation scanning of unknown variants, as well as genotyping of common variants. Concurrently, we have provided a list of methodical guidelines which could be applied for setting up HRM in other genetic laboratories and provided a diagnostic validation strategy for other DNA diagnostic techniques.

Furthermore, we have contributed to the higher quality of genetic services in the area of diagnostics of cystic fibrosis. This common life-threatening autosomal recessive disease is known for a substantial number of mutations in the CFTR gene and for its molecular heterogeneity based on the patient's ethnicity. Therefore, it is important to analyse mutation distribution and frequency of CFTR gene mutations among different populations.