Abstract

The characterisation of the molecular-genetic etiology of monogenic diseases includes not only the identification of the pathogenic variant, but also the description of its effect on the RNA structure and stability. Additionally, the X-inactivation plays an important role in X-linked diseases. In the presented thesis, we applied the methods of next generation sequencing to study three lysosomal disorders (mukopolysacharidosis type II, MPS II; Danon disease, DD; Fabry disease, FD). Two methodological approaches have been used: 1) panel sequencing with hybridization probes for identification of single nucleotide variants, small deletions/duplications and structure variants (CNVs) 2) amplicon sequencing for analysis of somatic mosaicism and allele specific expression.

The panel sequencing enabled us to confirm the molecular-genetic basis of DD in two patients with the identification of two exons duplication and five exons deletion in *LAMP2*, respectively.

The somatic mosaicism was being analyzed by the amplicon sequencing in families with DD, MPS II. We could identify the first case of somatic mosaicism in a patient with DD.

The allele specific expression has enlarged the group of methods used in X-inactivation analysis. Its impact has been proved particularly in minimizing misinterpretation of XCI results.

Results published in this thesis proved the importance of the next generation sequencing methods for the diagnosis of X-linked lysosomal storage disease, shedding light on their molecular basis leading to particular phenotype manifestation and even in determining their prognosis in selected cases.