Next generation sequencing technologies are changing the way scientific experiments and diseases diagnostics are performed and thus will allow what is called personalized medicine. The sense of presented thesis is to make survey of new approaches to DNA sequencing and demonstrate usage and constraints of bioinformatic analytical tools available to day. Discussed techniques are then applied to the case study of finding molecular basis for rare hereditary disease.

Introductory part deals with overview of commercially available sequencing techniques (454 Life Science, Applied Biosystems, Illumina, Helicos). Fundamentals of each method are described and possible further development is outlined. Post sequencing data analysis is than discussed in details.

In practical section we demonstrate genome analysis techniques successfully used to reveal causal mutation in the gene responsible for adult form of autozomal neuronal ceroid lipofuscinosis (ANCL). Combination of linkage analysis (Merlin), copy number variant analysis (Genome-Wide Human SNP Array 6.0), analysis of expression profiles (HumanRef-8 v2 Expression BeadChips) and exome sequencing (SOLiD™ 4 System) has been applied to members of one ANCL family. We also paid attention to comparison, evaluation and selection of available mapping algorithms used in reconstruction, analysis and anotation of sequencing data. Combined results from different techniques led to definition of small pool of genes localized in candidate areas defined by linkage analysis. Those genes have altered transcript profile in the patient tissue, they posses unique functionally important mutation and their known biological meaning could be linked to neuronal disease studied.

In the next step, candidate mutations have been confirmed by direct sequencing and their fenotype segregation have been checked up. Finally, we have found one mutation probably responsible for ANCL and its relevance is now under further study.