Abstract

Rare diseases (RD) are a heterogeneous group of diseases that affect about 5% of the world population. RDs represent more than 7.000 different phenotypes and many of them are genetically determined. RDs provide unique biological models for understanding the basic principles of molecular and cellular organization and function of human tissues and organs. Results of studies focused at pathogenesis of RDs are often used to diagnose and treat the affected patients. Significant progress in molecular genetic techniques, specifically the use of the next generation sequencing (NGS) in clinical practice, substantially facilitated and improved efficiency of RD laboratory diagnostics. Moreover, these novel testing algorithms identified the previously unknown molecular causes of many RDs.

This thesis demonstrates the utility of NGS techniques and bioinformatics processing of obtained data in studies aimed at understanding molecular basis of selected RDs. These methods led to identification and characterization of causative pathogenic variants in the *NDUFAF6* and *PLD1* genes among patients affected by the Acadian variant of Fanconi disease and patients with a rare congenital heart defect, respectively. This approach was further used to analyze exomes of a large cohort of patients with different types of cardiomyopathies. This part of the project characterized phenotypically different groups of patients and established accurate molecular genetic diagnosis in many of them.