

Abstract

Cancer the second most common causes of death in the Czech Republic. Carriers of mutations in genes predisposing to hereditary cancers represent a small but clinically significant group of high risk individuals. Today, dozens of predisposing genes for hereditary tumor syndromes are known and targeted next generation sequencing (NGS) has become a standard approach for their analysis. NGS allows rapid acceleration diagnostics of causal mutation in high-risk individuals. To identify mutations in genes predisposing to hereditary cancers, we designed a panel NGS analysis including subsequent bioinformatics analysis allowing a reliable identification of single nucleotide variants, insertions/deletions, and large intragenic rearrangements. The bioinformatics procedures described in this thesis were used for panel NGS validation, but also for identification of alterations associating with so far undescribed hereditary tumor types. Bioinformatics analyzes have become the basis for the unified processing of large datasets from the CZECANCA consortium and enable the construction of a population-specific database of genotypes that serve to improve clinical diagnostics of cancer predisposition in Czech patients. The versatility of NGS also allows its use for RNA (cDNA-based) analyzes of splicing variants in the genes of interest, which prerequisite for aberrant splicing identification.

Key words:

Hereditary cancer syndromes, next generation sequencing, bioinformatics analysis