

Abstract

Familial adenomatous polyposis (FAP) is a condition caused by germline mutations in tumor suppressor gene *APC*, inherited in autosomal dominant manner. Patients with FAP develop hundreds to thousands of adenomatous colorectal polyps with extremely high risk of malignant reversal into adenocarcinoma of colon and/or rectum.

The aim of this thesis is to re-analyze a cohort of highly suspected FAP probands from years 1993–2004 whose diagnosis previously failed to be confirmed by at that time commonly used methods of molecular diagnostics.

Next generation sequencing on MiSeq and NextSeq platforms (Illumina®) was performed on 78 samples of probands' DNA, isolated from peripheral blood, using gene panel CZEKANCA version 1.2 (Czech Cancer Panel for Clinical Application). The panel enables sequencing of exons and exon-intron junctions of 226 genes linked to hereditary cancer predispositions, newly also including the diagnostically important promoter 1B region of *APC*.

Pathogenic variant in the *APC* gene was detected in 18 % of re-analyzed probands, 11 % of probands carry pathogenic variants in other genes associated with colorectal polyps. Additional 13 % of probands are carriers of a variants of unknown clinical significance.

NGS gene panel CZEKANCA enabled diagnosis confirmation or re-evaluation of 22 FAP suspected probands. At least 5 detected variants in clinically significant genes represent new, not yet published and very probably pathogenic variants.