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Basic Study

Candidate colorectal cancer predisposing gene variants in Chinese early-onset and familial cases

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Abstract

AIM: To investigate whether whole-exome sequencing may serve as an efficient method to identify known or novel colorectal cancer (CRC) predisposing genes in early-onset or familial CRC cases.

METHODS: We performed whole-exome sequencing in 23 Chinese patients from 21 families with non-polyposis CRC diagnosed at ≤ 40 years of age, or from multiple affected CRC families with at least 1 first-degree relative diagnosed with CRC at ≤ 55 years of age. Genomic DNA from blood was enriched for exome sequences using the SureSelect Human All Exon Kit, version 2 (Agilent Technologies) and sequencing was performed on an Illumina HiSeq 2000 platform. Data were processed through an analytical pipeline to search for rare germline variants in known or novel CRC predisposing genes.

RESULTS: In total, 32 germline variants in 23 genes were identified and confirmed by Sanger sequencing. In 6 of the 21 families (29%), we identified 7 mutations in 3 known CRC predisposing genes including MLH1 (5 patients), MSH2 (1 patient), and MUTYH (biallelic, 1 patient), five of which were reported as pathogenic. In the remaining 15 families, we identified 20 rare and novel potentially deleterious