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Precision medicine: Role of rare mutation in colorectal cancer

Background & Aim: Several driver mutations have been discovered in colorectal cancer (CRC) progression including KRAS and BRAF that have practical significant therapeutic and prognostic value. Whole exome sequencing (WES) is revolutionizing screening for pathogenic single nucleotide variants (SNV) in complex disorders such as CRC. Little or no studies have comprehensively examined the association between somatic genetic variants in signaling pathways and risk of CRC in African Americans (AA). We aimed to determine somatic variants that drive colorectal carcinogenesis in AA.

Methods: WES was carried out on genomic DNA from 12 normal-tumor pairs of frozen biopsies from AA patients with CRC. For WES, base call quality recalibration, realignment around Indels, SNV calling and variants call recalibration were carried out using GATK (Genome Analysis Tool Kit) and normative population databases (e.g., 1000 Genomes SNP database, dbSNP and HapMap) provided the capability to filter genetic variants from putative mutations. Variants were then annotated using Annova. Sanger sequencing was used for validation of SNV.

Results: WES uncovered somatic mutations alteration in many genes that are known targets in CRC including *APC, BRAF, KRAS, Notch1, PIK3C2A* and *NDRG4*. We discovered a number of novel SNVs in *EID3, RGS3, HNRNPF, GNAS* and *APC* in tumor samples. We detected several rare and unique alterations in the known Wnt pathway gene: APC, MSH3 and ARID1. In addition, all three of these variants, APC4664, APC3418 and APC3862, are located in exon 15, which is the portion of APC most highly associated with CRC risk.

Conclusion: This work provides insight into identification of novel somatic mutations in *APC, MSH3* and *PIK3CA* from both Caucasian and African Americans with CRC. Our data suggest an association between specific genes in the Wnt signaling pathway and risk of CRC. The precise cancer genomes approaches may be effective in detecting CRC based on personalized medicine as a guide to develop more effective way for reducing cancer morbidity and mortality.

Biography

Hassan Ashktorab has completed his PhD from Utah State University and Postdoctoral studies from Indiana and University of Florida School of Medicine. He is the Director of Microarray and GI research group. He has published more than 95 papers in reputed journals and has been serving as an Editorial Board Member of repute journals. He has received the Outstanding Researcher Award in 2011 in Howard University College of Medicine. He is a Member of *PLoS One* and *Digestive Diseases and Science* Editorial Boards and past Editorial Board Member of Gut. He has been Member of different NIH study sections since 2002. He was awarded Visiting Professorship from Jiangsu University, China in 2015.

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