Medical Xpress

Schistosomiasis-associated colorectal cancer study yields unique insights into genetic mutations

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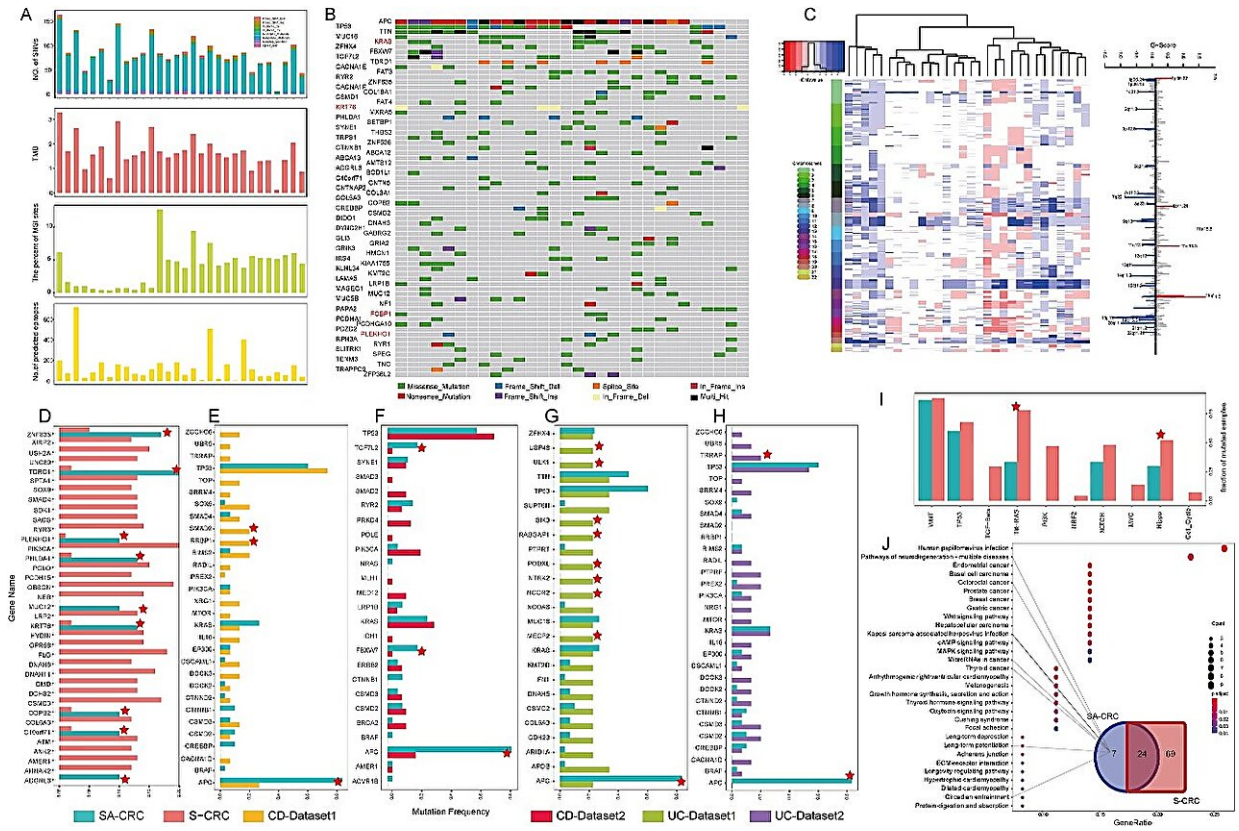

Genomic landscape of schistosomiasis-associated colorectal cancer. (A) Genetic characteristics of the SA-CRC. The number of mutations, the tumor mutation burden, the estimated MSI scores, and the predicted number of neo-epitopes of each sample were present. (B) Mutational landscape of recurrently mutated genes in SA-CRCs. Red arrow corresponds to the known driver gene, and the yellow arrow correspond to the novelly predicted driver genes. (C) Landscape of

somatic copy number alternations (SCNAs) in SA-CRCs. Heatmap of SCNAs across all the samples (left) and the significant enriched SCNA regions (right) were showed. (D) Recurrently mutated genes with significant differences in frequency between SA-CRC and S-CRC. Gold star denotes the genes highly mutated in SA-CRC. (E–H) Comparison of recurrently mutated genes in frequency between SA-CRC and other types of CRC. Red star denotes the genes showing significant differences in frequency between two datasets. (I) Comparison of known oncogenic signaling pathways in frequency between SA-CRC and S-CRC. (J) Dot plot of the conventional enriched pathways in SA-CRC. The small Venn plot shows the overlap of enriched pathways between SA-CRC and S-CRC. Credit: *Genes & Diseases*

In a study published in the journal *Genes & Diseases*, researchers from Naval Medical University and Soochow University conducted an in-depth investigation into the genomic landscape of schistosomiasis-associated colorectal cancer (SA-CRC).

By utilizing whole exome sequencing on tumor tissues and their non-tumor counterparts obtained from thirty SA-CRC patients diagnosed at Changzheng Hospital from 2014 to 2020, the team successfully identified 2476 nonsynonymous mutations spanning across 1978 genes. This intricate analysis revealed a lower median tumor mutation burden (TMB) in SA-CRC compared to sporadic colorectal cancer (S-CRC), suggesting SA-CRC is less responsive to immunotherapy due to its low microsatellite instability (MSI-L) or microsatellite stable (MSS) status.

Moreover, the team unearthed 71 recurrently mutated genes, including four newly discovered driver genes—KRT76 and PLEKHO1, whose mutation or deletion may play a crucial role in the pathogenesis of SA-CRC. A substantial number of somatic copy number alteration (SCNA) events were also found, predominated by copy number gain events. A comparison of the genomic profiles of SA-CRC with other types of

colorectal cancers (CRCs) shed light on the distinct genetic underpinnings of SA-CRC.

Interestingly, mutations typically found in S-CRC and inflammatory bowel disease-associated CRC, particularly in genes such as PIK3CA, ATM, and SMAD4, were notably infrequent in SA-CRC. Additionally, the study pinpointed two oncogenic signaling pathways, TGF-Beta and PI3K, that differ significantly between SA-CRC and S-CRC.

In a commendable effort to identify aggressive characteristics of SA-CRC, the research team scrutinized genomic alterations linked to patient outcomes, resulting in the identification of eight pivotal genes that may govern tumor progression and prognosis. These findings illuminate new pathways for future research, marking a significant stride in the understanding of SA-CRC.

It acknowledges limitations such as reliance solely on WES data and a relatively small sample size. Nonetheless, the study advances the understanding of the genomic landscape of SA-CRC and sheds new light on the pathogenesis of SA-CRC and its unique molecular profile, paving the way for future studies and treatment implications for this disease.

More information: Dong Yu et al, Genomic analysis of schistosomiasis-associated colorectal cancer reveals a unique mutational landscape and therapeutic implications, *Genes & Diseases* (2022). DOI: 10.1016/j.gendis.2022.05.026

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