Highly frequent gene mutations and co-occurring genes analysis in colorectal cancer (CRC)

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Background
Colorectal cancer (CRC) is the second most leading cause of cancer-related deaths worldwide. Understanding the molecular alterations that drive CRC is critical for improving patient outcomes. Next-generation sequencing (NGS) has revolutionized CRC molecular profiling by simultaneous analysis of multiple genes with high accuracy and sensitivity. In this study, we analyzed a cohort of CRC formalin-fixed paraffin-embedded (FFPE) samples to identify highly frequent gene mutations and co-occurring genes in CRC.

Methods
FFPE samples from CRC patients tested from January 2020 to December 2023 using NeoTYPE®-Colorectal Tumor Profile NGS assay were analyzed. NeoTYPE CRC profile NGS is a targeted next-generation sequencing focusing on a panel of 36 genes known to be frequently mutated in CRC. Patient demographics, sequence coverage, gene mutation frequency, exclusive mutation genes and clinical significance were explored and analyzed.

Overview of Study Workflow

Fig 1A: QIAseq DNA target panel NGS workflow

Results

Fig 2: Demographics of cohort testing. A: Gender distribution B: Age at sequencing

Fig 5: Six most frequently mutated genes consequence counts in CRC cohort. APC genes truncation mutations were the most prevalent while TP53, KRAS, PIK3CA and SMAD3 nonsense mutations were the major mutation category.

Key findings
- A total of 8,397 patients with CRC were included in this study (44% female, 56% male), with age group 61 to 80 years old exhibiting the highest prevalence.
- APC (39.2%), TP53 (25.2%), KRAS (16.1%), and PIK3CA (7.6%) were the most frequently mutated genes.
- The presence of APC mutations showed co-occurrence with KRAS and TP53 in our cohort.

Conclusions
- Our results suggest that the mutational landscape of CRC is complex, with multiple genes being affected in a coordinated manner.
- These findings can help in understanding the molecular mechanisms underlying CRC and thereby inform the development of novel therapeutic approaches for the treatment of CRC.