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RAS and PI3K Driver Mutations in Metastatic Colorectal Cancer: A Cohort Study of 60 Patients

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Abstract

Introduction: Metastatic Colorectal Cancer (MCRC) is now managed through personalized therapeutic strategies, guided by the identification of predictive biomarkers. The assessment of the mutational status of key genes, particularly RAS (KRAS/NRAS), is essential before initiating treatment. This study aimed to determine the prevalence of RAS and PI3K mutations in a cohort of mCRC patients and to correlate these findings with clinical and demographic data.

Methods: We conducted a retrospective, descriptive study over a 14-month period (December 2024 to January 2026), enrolling 60 patients with metastatic colorectal cancer. Molecular analysis was performed using PCR to detect mutations in KRAS, NRAS, and PI3K genes. Demographic and clinical data were collected from patient records.

Results: A total of 60 patients were included, with a mean age of 55 years (range: 32-86 years). The cohort comprised 32 males (53%) and 28 females (47%). Molecular analysis revealed:

- RAS wild-type status in 34 patients (56%);
- RAS mutations in 23 patients (38%), including 19 with KRAS codon 12 mutations (31%) and 2 with KRAS codon 13 mutations (3%);
- PI3K mutations in 2 patients (3%), both female.

Results were invalid in 3 patients due to insufficient material (1 male, 2 females). The overall prevalence of RAS mutations was 38%, consistent with international literature (30-45%).

Discussion: The observed prevalence of RAS mutations in our cohort (38%) aligns with previously reported data, reinforcing the importance of RAS screening in mCRC patients. The predominance of KRAS mutations in codon 12 highlights its role as a key oncogenic driver, influencing treatment response and prognosis. The low frequency of PI3K mutations (3%) suggests that alternative pathways may contribute to disease progression in this population. Invalid results underscore the challenges of sample quality in molecular testing.

Conclusion: This study confirms a high prevalence of RAS mutations in mCRC patients, supporting the routine use of RAS testing to guide personalized therapy. The predominance of KRAS codon 12 mutations emphasizes its clinical significance. Further research is warranted to explore the role of PI3K and other emerging biomarkers in therapeutic resistance.

Keywords: Metastatic colorectal cancer (MCRC); Biomarkers; RAS oncogene; KRAS mutation; Personalized therapy.

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Introduction

Colorectal Cancer (CRC) is the third most common malignancy worldwide, with metastatic disease (MCRC) accounting for a significant proportion of cases [1]. The management of mCRC has shifted toward precision oncology, driven by the identification of predictive biomarkers [2]. Among these, RAS gene mutations (KRAS/NRAS) are critical determinants of resistance to anti-EGFR therapies such as cetuximab and panitumumab [3,4]. Additionally, PI3K pathway alterations have been implicated in tumor progression and therapeutic resistance [5]. This study aimed to characterize the mutation profile of RAS and PI3K in a cohort of MCRC patients, providing insights for personalized treatment approaches.

Methods

Study design and population

We conducted a retrospective, single-center study enrolling 60 patients with histologically confirmed mCRC between December 2024 and January 2026. Inclusion criteria included: (1) diagnosis of mCRC, (2) availability of tumor tissue for molecular analysis, and (3) complete clinical records. Exclusion criteria included prior anti-EGFR therapy or inadequate sample quality.

Molecular analysis

DNA was extracted from Formalin-Fixed Paraffin-Embedded (FFPE) tissues. Mutations in KRAS (exons 2 and 3), NRAS (exons 2, 3, and 4), and PI3KCA (exon 9) were detected using PCR-based methods (e.g., Sanger sequencing or qPCR with allele-specific probes).

Statistical analysis

Descriptive statistics were used to summarize demographic and molecular data. Prevalence rates were compared with published literature using chi-square tests where appropriate.

Ethical considerations

This study was an analysis of anonymized patient data. As the research involved no direct intervention or modification of standard patient care, formal approval from an ethics committee was not required in accordance with institutional and national guidelines for observational studies. All patient data were anonymized prior to analysis to protect confidentiality.

Table 1: Baseline characteristics and molecular mutation profile of the study cohort.

Parameter	Value
Total patients	60
Male (n, %)	32 (53%)
Female (n, %)	28 (47%)
Mean age (years)	55 (32–86)
RAS wild-type (n, %)	34 (56%)
RAS mutated (n, %)	23 (38%)
KRAS codon 12 (n, %)	19 (31%)
KRAS codon 13 (n, %)	2 (3%)
PI3K mutated (n, %)	2 (3%)
Invalid results (n, %)	3 (5%)

Results

Patient characteristics

The cohort comprised 60 patients (53% male, mean age: 55 years). Clinical characteristics are summarized in (Table 1).

Mutation prevalence

The overall prevalence of RAS mutations was 38%, consistent with published data (30-45%) [6]. KRAS codon 12 mutations were the most common (31%), while PI3K mutations were rare (3%).

Discussion

The identification of driver mutations such as RAS and PI3K has revolutionized the management of metastatic colorectal cancer (MCRC), enabling the selection of patients most likely to benefit from targeted therapies. Our study, conducted in a cohort of 60 mCRC patients, revealed a RAS mutation prevalence of 38%, which aligns with the established range of 30-45% reported in international literature [6]. This consistency reinforces the robustness of RAS as a critical biomarker in clinical practice.

Clinical significance of RAS mutations

The predominance of KRAS mutations in codon 12 (31%) observed in our cohort underscores its role as a major oncogenic driver [7]. These mutations constitutively activate the MAPK pathway, leading to uncontrolled cell proliferation and resistance to anti-EGFR therapies such as cetuximab and panitumumab [3]. The low frequency of KRAS codon 13 mutations (3%) is consistent with previous studies, suggesting that codon 12 alterations are more prevalent in mCRC [7]. These findings highlight the importance of comprehensive RAS testing (including both KRAS and NRAS) to avoid missing actionable mutations.

Role of PI3K Mutations in MCRC

Although PI3K mutations were rare (3%) in our cohort, their presence may still have implications for treatment resistance and prognosis [8]. PI3KCA mutations, particularly in exon 9, have been associated with resistance to anti-EGFR therapies and potential sensitivity to PI3K inhibitors. Given the small number of PI3K-mutated patients in our study, further investigation in larger cohorts is warranted to clarify their prognostic and predictive value.

Limitations and challenges

Our study has several limitations. First, the retrospective design and small sample size (n=60) may limit the statistical power to detect rare mutations or subgroup differences. Second, the exclusion of patients with insufficient material (5%) introduces potential selection bias, emphasizing the need for standardized tissue collection protocols in molecular testing [9]. Third, the lack of longitudinal data on treatment response and survival prevents us from establishing a direct correlation between mutations and clinical outcomes. Future prospective studies with larger cohorts and integrated genomic profiling are needed to address these gaps.

Implications for personalized therapy

The high prevalence of RAS mutations in our cohort reinforces the necessity of routine biomarker testing before initiating

anti-EGFR therapy [3]. Additionally, the identification of PI3K mutations, albeit rare, suggests that comprehensive molecular profiling (including RAS, BRAF, PI3K, and HER2) may be beneficial for refining treatment strategies in mCRC. As new targeted agents emerge, the integration of Next-Generation Sequencing (NGS) into clinical practice could further improve personalized therapy.

Conclusion

This study confirms the high prevalence of RAS mutations in MCRC, supporting their established role as key biomarkers for treatment selection [3]. The predominance of KRAS codon 12 mutations reinforces its importance as an oncogenic driver [7], while the low frequency of PI3K mutations suggests that alternative pathways may contribute to disease progression in a subset of patients [8]. Although our findings align with existing literature [6], the limitations of our study highlight the need for larger, prospective investigations with integrated molecular and clinical data.

Moving forward, the implementation of comprehensive biomarker testing-including RAS, PI3K, and other emerging markers-will be crucial for optimizing personalized therapy in mCRC. Future research should focus on elucidating the functional consequences of rare mutations and their response to novel targeted agents, ultimately improving outcomes for patients with metastatic colorectal cancer.

Declarations

Conflicts of interest: The authors declare no conflicts of interest related to this article.

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Informed consent: This study had an anonymized patient data. As the research involved no direct intervention or modification of standard patient care, formal approval from an ethics committee was not required in accordance with institutional and national guidelines for observational studies. All patient's data were anonymized prior to analysis to protect confidentiality and treated according to the Algerian national guidelines

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References

1. Siegel R L, et al. CA Cancer J Clin. 2020; 70(1): 7-30.
2. André T, et al. Lancet. 2015; 385(9961): 120-130.
3. Douillard J Y, et al. N Engl J Med. 2014; 369(11): 1023-1034.
4. Van Cutsem E, et al. J Clin Oncol. 2011; 29(15): 2011-2019.
5. Dienstmann R, et al. Nat Rev Clin Oncol. 2014; 11(3): 138-149.
6. Karapetis C S, et al. N Engl J Med. 2008; 359(1): 175-180.
7. Di Fiore F, et al. J Clin Oncol. 2010; 28(1): 45-49.
8. Samuels Y, et al. Science. 2004; 304(5677): 976-979.
9. Prior T W, et al. Genet Med. 2012; 14(1): 70-75.