All about KRAS for clinical oncology practice: gene profile, clinical implications and laboratory recommendations for somatic mutational testing in colorectal cancer

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Source

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Abstract

The KRAS oncogene has been extensively studied for more than three decades, however, it is only recently that it attained a central role in the clinical decision-making process for the practicing oncologist. Recently, based on retrospective analyses of large randomized clinical trials, the use of anti-epidermal growth factor (EGFR) monoclonal antibodies, cetuximab and panitumumab, was restricted to patients with metastatic colorectal cancer that carry the "wild-type"KRAS genotype. Challenges remain in the laboratory implementation of KRAS mutational testing and the clinical application of the test for treatment planning. This review attempts to offer a global view of KRAS biology, its functional role in cell signaling, mechanisms of resistance to anti-EGFR agents and its predictive potential in metastatic colorectal cancer. We also survey the growing list of candidate biomarkers that may shortly supplement KRAS in routine clinical patient stratification. Finally, we discuss practical aspects of KRAS testing that may be useful for those involved in mutational screening in their centers. This general overview of KRAS for clinical oncology practice aims to assist in data interpretation and offer insight into potential pitfalls of mutational testing. KRAS is a prime example of how translational research can fulfill the promises of personalized medicine for tailoring treatment to match the underlying tumor biology.