

Review

The ideal reporting of *RAS* testing in colorectal adenocarcinoma: a pathologists' perspective

Umberto Malapelle¹, Valentina Angerilli², Francesco Pepe¹, Gabriella Fontanini³, Sara Lonardi⁴, Mario Scartozzi⁵, Lorenzo Memeo⁶, Gianfranco Pruneri⁷, Antonio Marchetti^{8,9}, Giuseppe Perrone^{10,11*}, Matteo Fassan^{2,12*}

¹ Department of Public Health, University of Naples Federico II, Naples (NA), Italy; ² Department of Medicine (DIMED), University of Padua, Padua (PD), Italy; ³ Department of Surgical, Medical and Molecular Pathology and Critical Care Medicine, University of Pisa, Pisa (PI), Italy; ⁴ Medical Oncology 3, Veneto Institute of Oncology IOV-IRCCS, Padua (PD), Italy; ⁵ Medical Oncology, University Hospital and University of Cagliari, Cagliari (CA), Italy; ⁶ Department of Experimental Oncology, Mediterranean Institute of Oncology, Viagrande, Catania (CT), Italy; ⁷ Department of Advanced Diagnostics, Fondazione IRCCS Istituto Nazionale Tumori and University of Milan, Milan (MI), Italy; ⁸ Center for Advanced Studies and Technology (CAST), University Chieti-Pescara, Chieti (CH), Italy; ⁹ Diagnostic Molecular Pathology, Unit of Anatomic Pathology, SS Annunziata Hospital, Chieti (CH), Italy and Department of Medical, Oral, and Biotechnological Sciences University "G. D'Annunzio" of Chieti-Pescara, Chieti (CH), Italy; ¹⁰ Department of Medicine and Surgery, Research Unit of Anatomical Pathology, Università Campus Bio-Medico di Roma, Roma, Italy; ¹¹ Anatomical Pathology Operative Research Unit, Fondazione Policlinico Universitario Campus Bio-Medico, Roma, Italy; ¹² Veneto Institute of Oncology (IOV-IRCCS), Padua (PD), Italy; * Equally contributed as last authors

Summary

RAS gene mutational status represents an imperative predictive biomarker to be tested in the clinical management of metastatic colorectal adenocarcinoma. Even if it is one of the most studied biomarkers in the era of precision medicine, several pre-analytical and analytical factors may still impasse an adequate reporting of *RAS* status in clinical practice, with significant therapeutic consequences. Thus, pathologists should be aware on the main topics related to this molecular evaluation: (i) adopt diagnostic limit of detections adequate to avoid the interference of sub-clonal cancer cell populations; (ii) choose the most adequate diagnostic strategy according to the available sample and its qualification for molecular testing; (iii) provide all the information regarding the mutation detected, since many *RAS* mutation-specific targeted therapeutic approaches are in development and will enter into routine clinical practice. In this review, we give a comprehensive description of the current scenario about *RAS* gene mutational testing in the clinic focusing on the pathologist's role in patient selection for targeted therapies.

Key words: colorectal cancer, precision medicine, *RAS*, biomarkers

Introduction

In the era of precision medicine, the implementation of testing for established predictive biomarkers has become a crucial step of therapeutic management of patients with advanced colorectal cancer (CRC) ¹.

Received and accepted: May 24, 2023

Correspondence

Matteo Fassan
 Department of Medicine (DIMED); Surgical Pathology Unit, University of Padua, via Gabelli 61, 35121 Padua, Italy
 Tel.: (+39) 049 8217931
 E-mail: matteo.fassan@unipd.it

How to cite this article: Malapelle U, Angerilli V, Pepe F, et al. The ideal reporting of *RAS* testing in colorectal adenocarcinoma: a pathologists' perspective. *Pathologica* 2023;115:137-147. <https://doi.org/10.32074/1591-951X-895>

© Copyright by Società Italiana di Anatomia Patologica e Citopatologia Diagnostica, Divisione Italiana della International Academy of Pathology

