that a considerable fraction of CRC LN metastases do not resemble the respective primary tumors. The reasons that may underlie these findings are fully described in our article, but in summary, we believe that a KRAS mutation can either be acquired during metastasis to the LNs, as in our study, or be part of a heterogeneous population of neoplastic cells that constitutes the bulk of the primary tumor. These results are of fundamental importance, because they may represent one of the resistance mechanisms interfering with the response of patients with KRAS-WT mCRC to anti-EGFR monoclonal antibody therapy. We have written this letter because we believe that our results should be taken into consideration if KRAS screening is used as a tool to select patients for administration of this type of therapy.

ACKNOWLEDGMENT

Supported by Portuguese Foundation for Science and Technology (PTDC/SAU-OBD/68310/2006).

Sérgio Velho
Institute of Molecular Pathology and Immunology of the University of Porto, Porto, Portugal

Carla Oliveira and Raquel Seruca
Institute of Molecular Pathology and Immunology of the University of Porto; and Faculty of Medicine, University of Porto, Porto, Portugal

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

REFERENCES


DOI: 10.1200/JCO.2008.20.1525; published online ahead of print at www.jco.org on December 1, 2008

In Reply: We thank Velho et al for their interest in our study, which showed a 95% concordance rate of KRAS and BRAF status between primary and metastatic sites of colorectal carcinomas.1 The authors refer to their previous study, in which they found a lower concordance rate (64%) between lymph node metastases and primary tumors in a cohort of 28 of 250 colorectal cancers.2 Possible explanations for the discrepancy between the two concordance rates may be, first, that our patient series included only patients with stage IV disease and that of Velho et al included patients with stage 0 to IV disease, and second, that in the latter study, KRAS status was not assessed in distant metastatic sites.

In addition to our findings, full concordance of KRAS status between primary tumors and distant metastases,3-5 and between primary tumors and regional lymph nodes,6 has been reported by independent investigators, supporting the notion that detection of a KRAS-activating mutation in either a primary or metastatic site is sufficient to exclude a patient from epidermal growth factor receptor–targeted monoclonal antibody therapies.

Andrea Sartore-Bianchi and Salvatore Artale
Falck Division of Medical Oncology, Ospedale Niguarda Ca’ Granda, Milan, Italy

Silvio Veronese and Marcello Gambacorta
Division of Pathology, Ospedale Niguarda Ca’ Granda, Milan, Italy

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

REFERENCES


DOI: 10.1200/JCO.2008.20.2358; published online ahead of print at www.jco.org on December 1, 2008

Salvatore Siena
Falck Division of Medical Oncology, Ospedale Niguarda Ca’ Granda, Milan, Italy