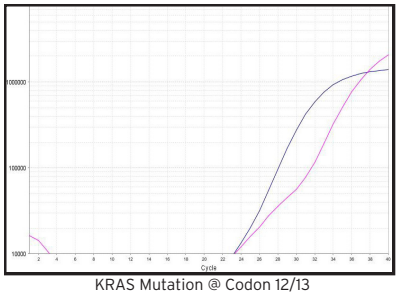
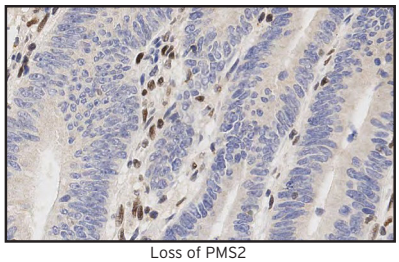
CSI Laboratories
Specialized Cancer Diagnostics

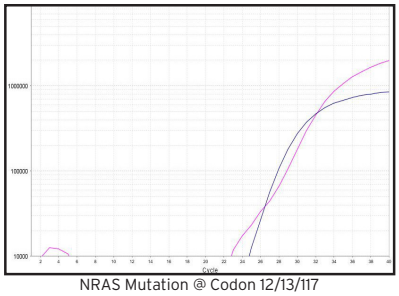
C•RESULTS Colorectal Carcinoma Panel

for Metastatic Colorectal Cancer (CRC)

KRAS, NRAS, BRAF by PCR & MMRP by IHC


KRAS Mutation @ Codon 12/13


Loss of PMS2


NRAS Mutation @ Codon 12/13/117

CSI Laboratories' CRC panel is a comprehensive diagnostic tool used to aid clinicians in the management of patients with colorectal cancer. The presence of KRAS, NRAS, or BRAF mutations in a confirmed case of colorectal cancer is associated with anti-EGFR inhibitor resistance. Limited therapies are available at this time for patients harboring these specific genetic mutations in the presence of CRC.

Extended KRAS & NRAS by Multiplex Real-Time PCR (Polymerase Chain Reaction)

CSI Laboratories provides clinically-validated, allele-specific PCR assays for the detection of either *KRAS* or *NRAS* mutations. These **extended panel** assays detect and differentiate between the most common *KRAS* and *NRAS* mutations in exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146). Both the KRAS Mutation Assay and the NRAS Mutation Assay have a sensitivity detection level of 2% mutant allele. In CRC patients, mutations of the *KRAS and NRAS* genes are generally associated with resistance to anti-*EGFR* therapy.[1]

**2017 CPT Code Billed by CSI Laboratories: 81275 & 81276 - KRAS Mutation Analysis*
**2017 CPT Code Billed by CSI Laboratories: 81311 - NRAS Mutation Analysis*

MMRP (Mismatch Repair Proteins) by IHC (Immunohistochemistry)

This IHC assay is utilized to identify patients who have a deficiency in DNA replication MMR genes: *hMLH-1, hMSH-2, hMSH-6,* and *PMS2*. Patients who show loss of one or more of the four DNA mismatch repair proteins (complete absence of nuclear immunoreactivity) should be further evaluated for Lynch Syndrome. Initial screening for Lynch Syndrome in all patients with colorectal carcinoma is recommended by the Evaluation of Genomic Applications in Practice & Prevention (EGAPP™) Working Group.[2]

**2017 CPT Code Billed by CSI Laboratories: 88342 x 1, 88341 x 3*

BRAF by Multiplex Real-Time PCR (Polymerase Chain Reaction)

CSI Laboratories provides a clinically-validated, allele-specific PCR assay for the detection of BRAF point mutations at V600E and V600K. CSI's BRAF Mutation Assay has a sensitivity detection level of 1% mutant allele. Based on the latest CRC guidelines, once a deficient MMRP protein is detected by IHC, then BRAF V600 mutation analysis can be performed, and if positive, this test strongly favors a sporadic CRC pathogenesis (BRAF mutation is rarely found in Lynch Syndrome-related CRCs).[4] However, the absence of BRAF mutation does not completely exclude the risk of Lynch Syndrome. Accordingly, testing for *MLH1 gene promoter hypermethylation* may then be activated, and if positive, favors a sporadic CRC pathogenesis.

**2017 CPT Code Billed by CSI Laboratories: 81210*

A promise that speaks to who we are.

- We will only recommend testing that is medically necessary and clinically significant.
- We will not base testing decisions on a patient's ability to pay.
- We will commit to investing in the latest technologies to ensure that you have the most precise results for your patients.

References

1. Douillard JY, Oliner KS, Siena S, et al. Pantimumab--FOLFOX4 treatment and RAS mutations in colorectal cancer. N Engl J Med 2013; 369:1023-1034.

2. Vasen HF, Blanco I, Aktan-Collan K, et al. Revised guidelines for the clinical management of Lynch syndrome (HNPCC): Recommendations by a group of European experts. Gut 2013;62:812-23.

3. Sharma SG, Gulley ML. BRAF mutation testing in colorectal cancer. Arch Pathol Lab Med. 2010;134(8):1225–1228.

4. Sepulveda AR, Hamilton SR, Allegra CJ, et al. Molecular biomarkers for the evaluation of colorectal cancer: guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology [published online ahead of print February 6, 2017]. Am J Clin Pathol.

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