CEDARS-SINAI MEDICAL CENTER
Pathology Services

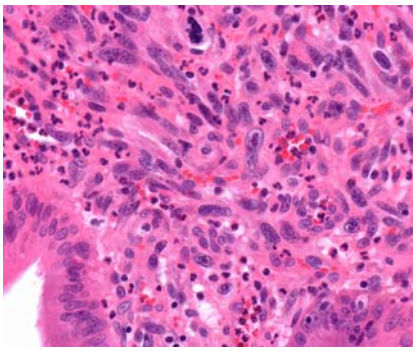
Immunohistochemical Detection of DNA Mismatch Repair Proteins in Colorectal Adenocarcinomas

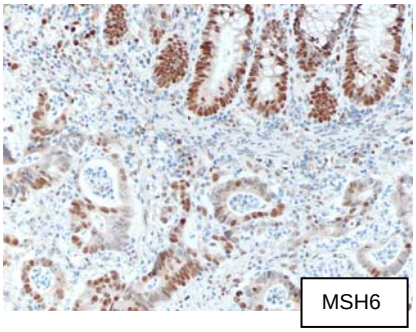
INTRODUCTION

- Provides immunohistochemical detection of four DNA mismatch repair proteins: MLH1, MSH2, MSH6 and PMS2
- Loss of nuclear expression of one or more of these proteins in tumor cells indicates the presence of microsatellite instability (MSI), which predicts a worse response to adjuvant chemotherapy, but consequently guides therapy to lead to improved overall survival

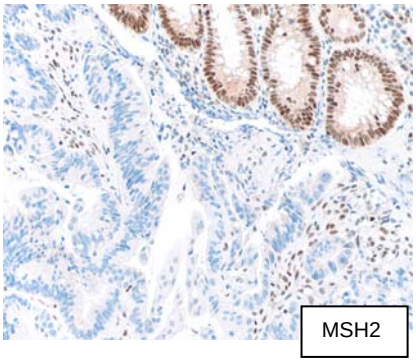
INDICATIONS

- Colorectal adenocarcinoma diagnosed before the age of 50 years
- Colorectal adenoma diagnosed before the age of 40 years
- Synchronous or metachronous colorectal or other HNPCC-related tumors, including those of the stomach, urinary bladder, ureter and renal pelvis, biliary tract, brain (glioblastoma) and small intestine, as well as sebaceous gland adenomas and keratoacanthomas, regardless of age
- Colorectal cancers diagnosed before the age of 60 years with morphologic features suggestive of MSI, such as tumor infiltrating lymphocytes, Crohn-like inflammatory response, mucinous or signet-ring cell differentiation, or medullary growth pattern
- Colorectal cancer with one or more first-degree relatives with colorectal or other HNPCC-related tumors. One of the cancers must have been diagnosed before the age of 50 years (this includes adenoma, which must have been diagnosed before the age of 40 years
- Colorectal cancer with two or more relatives with colorectal or other HNPCC-related tumors, regardless of age





MSH6



MSH2

SPECIMEN REQUIREMENTS

Formalin-fixed, paraffin-embedded tissue sections or blocks containing both tumor and nonneoplastic colonic mucosa are obtained

CONSULTATIVE SERVICES PROVIDED

- Perform IHC detection of MLH1, MSH2, MSH6, and PMS2
- Use IHC detection of these proteins to detect MSI

CONSIDERATIONS

- 90-95% sensitive comparing to PCR-based analysis
- Positive test (loss of protein expression) does not discriminate germline versus somatic DNA mismatch repair gene mutations
- Negative test (normal protein expression) does not entirely exclude HNPCC

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