**Sample MSS/MSI-L/IHC Normal Expression Report**

**Reason For Referral**

Possible diagnosis of Hereditary Nonpolyposis Colon Cancer (HNPCC)/Lynch syndrome. Evaluate tumor tissue for evidence of defective DNA mismatch repair.

**Method**

Immunohistochemical staining (IHC) is used to determine the presence or absence of protein expression for MLH1, MSH2, MSH6 and PMS2. Lymphocytes and normal epithelium exhibit strong nuclear staining and serve as positive internal controls for staining of these proteins. A PCR based assay is used to test for tumor microsatellite instability (MSI) with the use of 5 mononucleotide repeat markers. The tumor tissue is classified as MSS/MSI-L (instability detected in 0 or 1 out of 5 markers), or MSI-H (instability in 2 or more of 5 markers tested).

**RESULTS**

Tumor type: colon adenocarcinoma

IHC: Normal expression of MLH1, MSH2, MSH6, and PMS2

MSI: MSS/MSI-L (instability observed in 0 of 5 informative markers)

**Interpretation**

The combination of normal protein expression and an MSS/MSI-L phenotype suggests the presence of normal DNA mismatch repair function within the tumor. Thus, the likelihood that this individual has an inherited colon cancer syndrome due to defective DNA mismatch repair (HNPCC/Lynch syndrome) is reduced but not eliminated. However, these results do not rule out the possibility that this individual's tumor is due to an inherited defect in another gene not involved in DNA mismatch repair. A significant fraction of clinically defined HNPCC cases (30% or more) do not have defective DNA mismatch repair as the underlying genetic basis of their disease. Additionally, we cannot rule out the possibility that this individual or family has HNPCC/Lynch syndrome because this tumor could represent a sporadic occurrence. If there is a strong personal or family history of HNPCC/Lynch syndrome related cancers for this patient or if this individual has multiple tumors, consider microsatellite instability (MSI) and immunohistochemical staining (IHC) on a different tumor to further evaluate the possible role of defective DNA mismatch repair for this individual or family. Of note, the literature suggests that MSI analysis on neoadjuvant chemoradiated tumor specimens may influence MSI status and lead to an erroneous interpretation of results (Int J Radiat Oncol Biol Phys. 2007 68(5):1584). Due to the sensitivity of the method being used, microsatellite instability cannot be reliably detected in samples containing less than 30% tumor DNA. Samples are routinely macrodissected to enrich for tumor cells, with those less than 30% rejected from further testing. A genetic consultation may be of benefit.

**CAUTIONS**

Test results should be interpreted in context of clinical findings, family history, and other laboratory data. If results obtained do not match other clinical or laboratory findings, please contact the laboratory for possible interpretation. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.