

Alerting on Hepatic Metastasis Predisposition: Liver Prometastatic Reaction Gene Profiling Test

- Currently, most of malignant tumors are now detected and treated at early stages, but metastases are still the main cause of cancer-related mortality. The liver is one of the most commonly involved sites, both in adult and child malignancies. This is in part due to the favorable microenvironment for metastatic cancer cell homing and growth (1), generated by the strong inflammatory, immune-tolerant and regenerative reactions of liver cells during cancer growth (2).



- Therefore, the acquired hepatic predisposition to metastatic recurrence is the result of a functional interplay between hepatic pathophysiology and cancer phenotype in each patient (3), and it has been named as the “liver prometastatic reaction” (3). However, it is highly heterogeneous among patients with and without cancer. It depends in part on the patient’s genetic and physiologic background, and in part on the stimulating effects of circulating soluble factors delivered from remote primary tumors and acting on the liver (4-6). Whatever the cause of metastasis propensity enhancement is, it normally develops in the liver prior to primary CRC removal, and therefore can be studied in liver biopsies obtained during CRC surgery (4-7).
- PBM has now developed a novel and sensitive laboratory test to determine the liver prometastatic reaction at a gene expression level, in hepatic biopsies from CRC patients without clinically-detectable hepatic metastases. A customized TaqMan-low density expression array to perform relative quantitation of the expression level and transcriptional association pattern of key genes from the liver prometastatic reaction, is used. In addition, an algorithm-based software processing gene expression data in conjunction with clinical

and anthropometric parameters of the patient is finally used to predict metastatic recurrence in the liver.

- The transcriptional test is helpful for prognosticating, monitoring and even preventing hepatic metastasis recurrence in patients with resected gastrointestinal malignant tumors, but also with non-gastrointestinal malignancies at risk of hepatic metastasis recurrence such as lung, adrenal, prostate and breast cancers, melanoma and sarcoma. It may also be helpful for predicting time to recurrence and post-recurrence survival in patients who undergo primary curative hepatectomy for the resection of CRC metastases. The test is also recommended for patients with invasive CRC whose potential hepatic metastases could not be detected by conventional imaging (8-9).
- Positive and negative results of the tests should be interpreted in conjunction with all other available examinations on invasive CRC. Positive test results should be referred to other independent risk factors and clinical prognostic parameters of liver metastasis for confirmation, and may suggest upstaging of the CRC according to conventional staging system, allowing physicians to decide on administration of neoadjuvant therapy or prophylactic adjuvant hepatic arterial infusion chemotherapy for prevention of hepatic metastasis development. A negative test result does not guarantee absence of CRC metastasis risk and patients should continue participating in a micrometastasis screening program at an interval and with a method appropriate for the individual patient.
- This test has been developed and its clinical performance features determined by PBM. It has not been cleared or approved by the FDA. It should not be regarded as investigational or for research. Final diagnosis and optimal patient management are the responsibility of the referring physician or health care provider.

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