

Abstract accepted for publication: Annual Meeting of American Society of Clinical Oncology, Chicago, May 30 - June 3, 2008

## **A Gene Expression Microarray-Based Diagnostic Test Applied to Patients with Carcinoma of Unknown Primary (CUP)**

Medeiros, Fabiola, M.D.; Kolbert, Christopher P.; Rakhshan Rohakhtar, Fariborz; Kane Lindgren, Tina M.; Wilson, Marcia J.; Rigl, C. Ted, Ph.D., Goetz, Matthew P., M.D.; Henner, David W., M.D., PhD; Halling, Kevin C., M.D., Ph.D.

**Background:** The workup of tumors presenting as metastatic disease is often laborious and expensive; many malignancies remaining unclassified as to site of origin. A gene expression test has been validated as an identifier of tissue of origin using metastatic tumors in which the primary site is known (Monzon 2007, Dumur 2008). Agreement with pathologist-issued diagnoses was 89.5% (95% CI 86.4 - 92.1%, n = 477). The test is not cleared by the FDA and was not validated in patients with CUP. We sought to determine the diagnostic performance of this test using CUP specimens from the Mayo Clinic tissue bank.

**Methods:** Eleven fresh-frozen tumor biopsies derived from patients with CUP were processed with the Pathwork® Tissue of Origin (TOO) Test (Pathwork Diagnostics, Sunnyvale, CA). The TOO Test uses expression signals from 1,550 probe sets to quantitatively measure the similarity of tumor specimens to 15 tissues of origin. Each patient previously underwent a full clinical and imaging workup; tissue specimens were previously thoroughly evaluated, including extensive immunohistochemistry, with no determination of site of origin. TOO test results were compared with clinical, radiologic and pathologic findings.

**Results:** Of the 11 CUP specimens, 8 (73%) were positive for one of the 15 tissues on the panel and 3 (27%) were indeterminate. In 6 of the positive calls (4 colorectal, 2 ovarian), the result was consistent with the clinicopathologic differential. In 2 cases, the TOO result was unexpected but strongly indicated breast and lung primaries, respectively. On average, 12 tissues per specimen could be eliminated as potential tissue of origin with high probability.

**Conclusions:** The Pathwork Tissue of Origin (TOO) Test successfully indicated a probable origin of metastatic carcinomas in 73% of the specimens tested. We conclude that this test has the potential to aid in the diagnosis of cancer patients presenting with metastatic carcinomas of unknown primary (CUP). The workup of tumors presenting as metastatic disease is often laborious and expensive; many malignancies remaining unclassified as to site of origin. A gene expression test has been validated as an identifier of tissue of origin using metastatic tumors in which the primary site is known (Monzon 2007, Dumur 2008). Agreement with pathologist-issued diagnoses was 89.5% (95% CI 86.4 - 92.1%, n = 477). The test is not cleared by the FDA and was not

validated in patients with CUP. We sought to determine the diagnostic performance of this test using CUP specimens from the Mayo Clinic tissue bank. Eleven fresh-frozen tumor biopsies derived from patients with CUP were processed with the Pathwork® Tissue of Origin (TOO) Test (Pathwork Diagnostics, Sunnyvale, CA). The TOO Test uses expression signals from 1,550 probe sets to quantitatively measure the similarity of tumor specimens to 15 tissues of origin. Each patient previously underwent a full clinical and imaging workup; tissue specimens were previously thoroughly evaluated, including extensive immunohistochemistry, with no determination of site of origin. TOO test results were compared with clinical, radiologic and pathologic findings. Of the 11 CUP specimens, 8 (73%) were positive for one of the 15 tissues on the panel and 3 (27%) were indeterminate. In 6 of the positive calls (4 colorectal, 2 ovarian), the result was consistent with the clinicopathologic differential. In 2 cases, the TOO result was unexpected but strongly indicated breast and lung primaries, respectively. On average, 12 tissues per specimen could be eliminated as potential tissue of origin with high probability. The Pathwork Tissue of Origin (TOO) Test successfully indicated a probable origin of metastatic carcinomas in 73% of the specimens tested. We conclude that this test has the potential to aid in the diagnosis of cancer patients presenting with metastatic carcinomas of unknown primary (CUP).