

## Utility of Gene Expression Profiling for Reporting Difficult-to-Diagnose Cancers

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Poster Presented at the Association for Molecular Pathology Annual Meeting, November 2011, Grapevine, TX

### BACKGROUND

Studies of primary and metastatic lesions of poorly differentiated malignancies find approximately 80% of lesions are identified with routine stains and immunohistochemistry (IHC). When examining only metastatic carcinomas of unknown primary, this figure drops to 65%. Limited clinical information further decreases this value. Inexperienced pathologists will arrive at erroneous conclusions more frequently. When the primary tumor site is ambiguous among three or more possibilities, there are no standard algorithms for IHC panels. Information from these stains is often indeterminate. The appropriate use of targeted chemotherapy requires knowledge of tumor type. These expensive therapies have side-effects and are only effective for select patients. A determination of primary tumor is requisite for their use. Pathwork Diagnostics® offers a Tissue-of-Origin® Test as an adjunct to IHC to reduce ambiguity of stain interpretation and provide greater accuracy in determination of cancers of unknown origin.

### METHODS

This is a retrospective study of cases referred for Tissue of Origin Testing from April 1, 2009 through the present. Cases included have histopathology reports and three or more possible sites of origin. Original diagnosis, Tissue of Origin results, and difference, if any, between working and final diagnoses are compared. Tissue of Origin Testing relies on mRNA expression in 15 organs. 2,000 mRNA sequences compile the expression profiles. Tumors are given a similarity score, ranging from 0-100, to a particular tissue based on mRNA sequences. The scores sum to 100 across tissue types. A high score confidently determines tumor origin. Scores under 20 are non-contributory. Tumor types with scores under 5 can be ruled out with >99% confidence.

### RESULTS

Twenty-three cases of difficult-to-diagnose carcinomas were examined for original working diagnoses, gene-expression profiling (GEP) and difference in final opinion based on GEP results. In 15/23 GEP revealed a different site of origin from the original working diagnosis, with 13/15 producing a change in final opinion. Interestingly, in 2/13 of these cases a clinically assumed primary lesion proved to be metastatic, resulting in a higher clinicopathologic stage. In 2/15 the similarity score was not high enough to change the pathologists' final assessment. For 2/23 the GEP similarity score was below 20, the lowest meaningful score, resulting in no diagnostic significance. The remaining 6/23 cases had GEP results that concurred with the original interpretation.

### DISCUSSION

The Pathwork Diagnostic® Tissue of Origin Test is a valuable adjunct to immunohistochemistry in determining site of origin for lesions that are poorly differentiated or show staining and morphology patterns that are inconsistent with expectation. Given the current clinical need for origin determination, the Tissue of Origin Test can provide increased diagnostic acumen for challenging specimens.

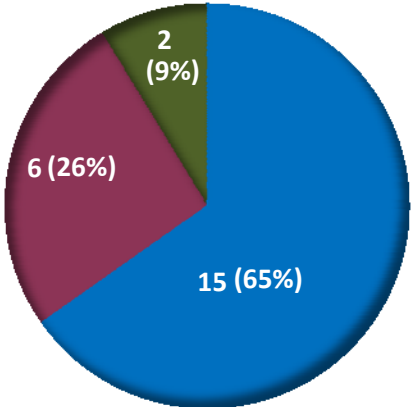
### REFERENCES

- 1.) Anderson GG, Weiss L. Determining Tissue of Origin for Metastatic Cancers Meta-analysis and Literature Review of Immunohistochemistry Performance. *Appl Immunohistochem Mol Morphol*. Volume 00, Number 00, 2009.
- 2.) Hornberger J, Mahul A, Varadhachary G, Henner WD, Nystrom JS. Effect of a gene expression-based Tissue of origin Test on patient management for difficult-to-diagnose primary cancers. American Society of clinical Oncology. 2011 Gastrointestinal Cancers Symposium. Jan 2011.

***For information about the Pathwork® Tissue of Origin Test, please contact Pathwork Diagnostics at [Info@Pathworkdx.Com](mailto:Info@Pathworkdx.Com) Or Call 1-877-808-0006***

# Tissue of Origin Test Results Compared to Original Working Diagnoses:

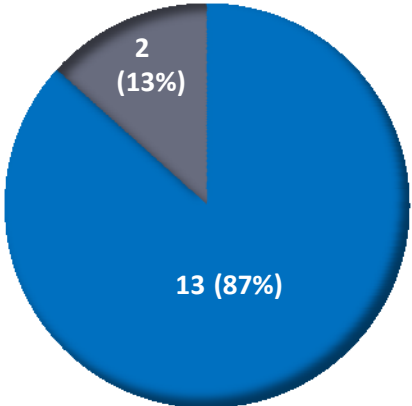
N = 23



- DISCORDANT WITH ORIGINAL WORKING DIAGNOSIS
- CONCORDANT WITH ORIGINAL WORKING DIAGNOSIS
- INCONCLUSIVE

## Resolution for Discordant Diagnoses:

N = 15



- FINAL DIAGNOSIS CHANGED FROM ORIGINAL WORKING DIAGNOSIS
- FINAL DIAGNOSIS UNCHANGED FROM ORIGINAL WORKING DIAGNOSIS