ONCOblot Reports

MorNuCo Inc., Purdue Research Park, 1201 Cumberland Ave, W Lafayette, IN 47906
To subscribe, e-mail: processing@oncoblotlabs.com

Volume 1, No. 2
June, 2015

Primary Tumors and Distant Metastases Produce Identical ENOX2 Protein Transcript Variants that Aid in the Identification of Cancers of Unknown Primary

David J. Taggart

MorNuCo, Inc. is pleased to continue the electronic publication of a new series of monthly reports for participating physicians and health professionals dealing with developing areas and extant questions relating to the ONCOblot® Tissue of Origin Cancer Test. In this issue, the ability of the ONCOblot® Test to identify the primary tissue of cancer origin with respect to distant metastases and cancers of unknown primary (CUP) is addressed.

The ONCOblot Test Aids Identification of Cancers of Unknown Primary (CUP)

Defining the tissue of origin of a cancer of unknown primary (CUP) is one of the more challenging tasks faced by oncologists (1, 2), especially when pathological examination of the tissue of a poorly differentiated metastatic tumor does not yield a definitive result. In these cases, the ONCOblot® Tissue of Origin Cancer Test may offer significant assistance in the identification of the tissue of origin of a primary cancer through the detection of tissue-specific ENOX2 proteins in patient serum. Based upon the analysis of sera samples from over 800 clinically-confirmed, primarily late stage cancer patients, the ONCOblot test is capable of detecting tissue-specific ENOX2 protein transcript variants that are sufficiently distinct to allow for the identification of 24 separate tissues of primary cancer origin.

Primary and Metastatic Tumors Produce Identical ENOX2 Protein Markers

Metastases occur when malignant cells are shed from a primary tumor and travel through either the blood or the lymph system to distant sites in the body. These malignant cells then possess the potential to establish new tumors, referred to as metastatic tumors. Although metastatic tumors develop at sites distant from the primary tumor, these metastatic tumors retain the phenotype and cell surface markers of the primary tumor (3), as the metastatic tumor cells are initially genetically identical to the cells of the primary tumor (4).

Consistently, both metastatic tumors and the primary cancers from which they are derived produce identical ENOX2 protein transcript variants, which are then shed into blood serum. Therefore, detection of ENOX2 protein transcript variants shed by either a primary cancer or its distant metastases will

yield similar ONCOblot® test results. For example, if a primary breast cancer has metastasized to the lung, only ENOX2 transcript variants indicative of breast cancer will be produced by both the primary and the distant metastasis, which share a common tissue of origin. This observation is supported by the finding that serum from subjects that were clinically diagnosed with either a single primary tumor or a primary tumor with distant metastases only contained ENOX2 transcript variants indicative of the tissue of primary cancer origin (5). Importantly, if two or more primary cancers are simultaneously present within a subject, ENOX2 transcript variants indicative of each tissue of primary cancer origin will be expressed and shed into the blood serum.

As with other serum cancer marker tests, the ONCOblot® test does not reveal if a primary cancer has metastasized or indicate where in the body a metastatic tumor may be located. Instead, the primary role of the ONCOblot® test is to identify the primary tissue of origin of any cancers that are present through the detection of tissue-specific ENOX2 protein transcript variants shed into blood serum.

Summary

Metastatic tumors located at distant sites are derived from cells that were shed from the primary cancer and therefore, produce identical ENOX2 protein transcript variants as the primary cancer. Since the ONCOblot test differentiates among 24 different tissues of origin, the test has the potential to aid in the identification of cancers where the tissue of origin is not known.

References

1. Pavlidis N. Cancer of unknown primary site. *Lancet*. 2012;379(9824):1428-1435
2. Varadhachary GR, Raber MN. Cancer of Unknown Primary Site. *N Engl J Med*. 2014;371(8):757-765.
3. Connolly JL, Schnitt SJ, Wang HH, et al. Role of the Surgical Pathologist in the Diagnosis and Management of the Cancer Patient. In: Kufe DW, Pollock RE, Weichselbaum RR, et al., editors. Holland-Frei Cancer Medicine. 6th edition. Hamilton (ON): BC Decker; 2003.
4. Greaves M, Maley CC. Clonal Evolution in Cancer. *Nature*. 2012;481(7381):306-313.
5. Hostetler B, Weston N, Kim J, et al. Cancer-Site-Specific Isoforms of ENOX2 (tNOX), a Cancer-Specific Cell Surface Oxidase. *Clin. Proteomics*. 2009;5(1):46-51.