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Expression of the ENOX2 Serum Cancer Marker in Advance of Clinical Symptoms

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MorNuCo, Inc. continues its monthly report for participating physicians and health professionals in order to answer common questions relating to the ONCOblot® Tissue of Origin (Cancer) Test.

The ONCOblot® Tissue of Origin Test is based upon the detection of tissue-specific protein transcript variants of ENOX2, a cancer-specific cell surface protein that is shed into the circulation. Recently, a retrospective analysis of serum samples from asbestos-exposed individuals who were eventually diagnosed with malignant mesothelioma was completed (1). This retrospective analysis was the first published evidence that ENOX2 could be detected within a patient population, 4-10 years in advance of a clinical diagnosis of mesothelioma. Although asbestos-induced malignant mesothelioma is characterized by a long latency period (the time between carcinogen exposure and clinical diagnosis of cancer) and is often diagnosed only in the late stages of disease progression, the production of detectable amounts of ENOX2 during early stages of disease progression may be a trait of many, and perhaps all, cancer types. Here, we provide further evidence that is consistent with the conclusion that the ENOX2 serum cancer marker can be detected in advance of clinical symptoms for cancers of different tissues of origin.

The possibility that a two-dimensional gel and western blot system may be able to detect ENOX2 in advance of clinical symptoms was first implied from findings with a special lung cancer panel of sera specimens obtained through the Early Detection Research Network (EDRN) of the National Cancer Institute. This panel consisted of 20 serum samples from patients with clinically-confirmed lung cancer and 35 serum samples from subjects with a history of smoking, but who were not diagnosed with cancer at the time of serum collection. All 20 of the known lung cancer patient sera contained an ENOX2 protein transcript variant indicative of lung cancer presence. However, a high incidence (17/35) of lung cancer-specific ENOX2 proteins were also found within serum samples from individuals who were smokers, but who were not diagnosed with cancer at the time of the serum draw. Of these serum samples, 16/17 of the subjects were smokers in the high range of 15-88 pack-years (the number of packs smoked/day multiplied by number of years smoked). The anticipated incidence of undetected lung cancers in such a population would normally be in the order of 10% rather than nearly 50%. Since the detected ENOX2 isoforms were a single molecular species that is also detected in serum samples of clinically-confirmed lung

cancer patients, these findings are consistent with a conclusion that lung cancer-specific ENOX2 protein transcript variants were being detected years in advance of the onset of clinical symptoms, which is in keeping with the results of the recently published mesothelioma study (1). This estimate assumes a 20-year development time for lung cancer between carcinogen exposure and the diagnosis of a clinically evident cancer (2) as diagrammed in Figure 1.

Similar results were obtained with a panel of female subjects at risk for breast and ovarian cancer. A panel of 127 serum samples in a Biomarker Reference Set for Cancers in Women also provided through the EDRN was analyzed. The panel consisted of samples pooled from 441 women in 12 different gynecologic and breast disease categories plus 115 sera from age-matched women with no diagnosis of cancer. Of the 127 sera samples in the panel, 29 contained a breast cancer-specific form of ENOX2 and 16 contained ovarian cancer-specific forms of ENOX2. These findings suggest that ENOX2 protein transcript variants were being detected in the control population much earlier than other serum cancer markers. As estimated for lung cancer, the presence of cancer-specific ENOX2 protein transcript variants may also be detected years before clinical symptoms based on the 20-year development time estimated between a breast cancer causing event and a clinical diagnosis of breast cancer (3) as diagramed in Figure 1.

Importantly, cancers progress at different rates, and the ENOX2 serum cancer marker is not expected to be detected years in advance of clinical symptoms for every individual. The utility of the ENOX2 cancer marker within asymptomatic populations is still being determined.

References

1. Morré DJ, Hostetler B, Taggart DJ, Morré DM, Musk AW, Robinson BW, Creaney J. (2016) ENOX2-based early detection (ONCOblot) of asbestos-induced malignant mesothelioma 4-10 years in advance of clinical symptoms. Clin Proteomics. 13:2.
2. Petro R, Darby S, Deo H, Silcocks P, Whitley E, Doll R (2000) Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case-control studies. Br Med J 321:323-329.
3. Weinberg RA (2007) the Biology of Cancer, Fig. 11.1, p, 400. Courtesy of Hong, W.K., compiled from SEER Cancer Statistics Review, Garland Science, Oxford.
4. Morré DJ. Morré DM (2013) ECTO-NOX Proteins. Springer, 505 pp.

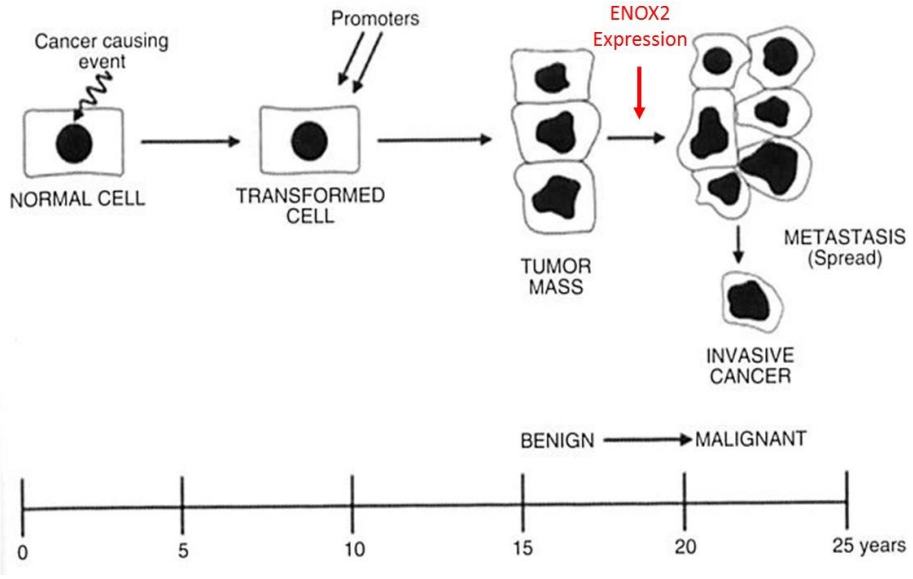

Figure 1. Interpretive diagram of the various stages of cancer progression (estimated to require as long as 20 years) beginning with a cancer-causing event (initiation) through development of a clinically defined malignancy. Reproduced from Morré and Morré 2013 (Ref. 4) with permission from InTech.