ONCOblot Reports

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Estimation of the Accuracy of the ONCOblot® Tissue of Origin Cancer Test

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MorNuCo, Inc. is pleased to announce 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 inaugural issue, the question of the accuracy of the ONCOblot® test is addressed. Future issues will address possible subtypes within major tissues of origin, tissues of origin in relation to distant metastases and clinical evidence from longitudinal studies as well as comments from physicians.

The ONCOblot® Tissue of Origin Cancer Test is an *in vitro* diagnostic intended to measure the degree of similarity between expression of ENOX2, a cancer-specific protein marker shed into human sera, and the ENOX2 protein expression patterns in a data base of serum samples from subjects with cancers clinically diagnosed according to then-current clinical and pathological practice.

The original data base (01/01/2013) contained 804 entries. Data were from sera of clinically diagnosed, primarily late stage, cancer patients from sources including the following: Greater Baltimore (Maryland) Cancer Center, Goshen (Indiana) Cancer Center, Early Detection Research Network of the National Cancer Institute, Novagen (North Ryde, Australia), Illinois Leukemia Society, Indiana University (Indianapolis), Hanau Medical Group (West Lafayette, Indiana) and Horizon Cancer Center (Lafayette, Indiana). Of these serum samples from patients reported to have clinically diagnosed cancer, two failed to yield ENOX2 transcript variants indicative of cancer. Both were reported as breast cancer (2 out of 291 breast cancer entries analyzed or 0.7%). The current data base (4/29/2015) consists of 1587 entries with no additional false negatives.

Definition of a False Positive

A false positive is the detection of an in range ENOX2 transcript variant from a cancer-free individual that fails to appear upon subsequent analyses of the same serum sample. For the most recent 1500 ONCOblots® carried out according to current protocols, only one ONCOblot® result has been confirmed as a false positive (0.06%).

Definition of a False Negative

A false negative is the absence of an in range ENOX2 transcript variant from an individual with clinical symptoms arising from a clinically diagnosed (pathology) cancer, present at the time of testing and at an ENOX2 concentration above the limit of detection of the assay. For the most recent 1500 ONCOblots® carried out according to current protocols, only ten ONCOblot® results have been confirmed or suspected false negatives (0.6%).

Limit of Detection

As with any diagnostic test, there is a lower limit of detection currently set at 200 femtomoles of ENOX2. This amount of ENOX2 is estimated to be produced by about 2 million cancer cells in the body, which is equivalent to a solid tumor 0.8 to 1.2 mm in diameter.

Misidentification of the Tissue of Origin

For several cancers, two or more ENOX2 transcript variants must be present within the ONCOblot® Tissue of Origin Cancer Test to permit the correct identification of the tissue of origin. These include bladder, colorectal, gastric, mesothelioma, ovarian, renal cell and uterine cancer. If one or more ENOX2 transcript variants are absent or below the limit of detection, the tissue of origin of the cancer may be misidentified. For the 1,587 late stage cancers currently in the data base, 53 (3.3%) would have been misidentified on the basis of a missing transcript variant. Missing ENOX2 proteins may be more prevalent with early stage cancers.

There were 32 examples of suspected or documented indications of an incorrect diagnosis out of the most recent 1500 ONCOblots® analyzed under our current protocol for a misidentification rate of 2.8%, very close to that of 3.3% predicted from the estimate based on the data base entries above.

Summary

In this ongoing analysis of the accuracy of the ONCOblot® Tissue of Origin Cancer Test, representing the most recent 1500 tests completed under the current protocol, the incidence of confirmed false positives and confirmed false negatives is low, less than 1% each. The major source of error, approximately 3%, is misidentification of the tissue of origin. The latter is most prevalent with colorectal, ovarian, renal cell and uterine cancers where two or more ENOX2 transcript variants are required for identification of the tissue of cancer origin. Thus, the overall sensitivity of the test with clinically diagnosed cancers may be greater than 95%, but more testing is needed to accurately determine the rate, especially at or near the limit of detection of the assay.