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Para Neoplastic Antigens as Biomarkers for Early Detection and Prediction of Recurrence of Ovarian Cancer

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Editorial Note

Pneumoconiosis Routine disease monitoring of ovarian cancer patients is generally recommended by gynecologic oncologists for women from high-risk families and for ovarian cancer patients during after the completion of primary surgery and first-line chemotherapeutic treatments. The recurrence is determined by measuring the level of serum CA125, one of the most extensively used tumor biomarkers in standard clinical practice for disease surveillance. Numerous studies have shown the role of tumor autoantibodies as biomarkers for ovarian cancer diagnosis and its recurrence. These autoantibodies to Tumor Associated Antigens (TAAs) arise due to the generation of humoral immune response before evidence of clinical symptoms in cancer patients. Previously we showed that a 3 biomarker panel predicted ovarian cancer recurrence at a median lead time of 9.07 months with 94.7% sensitivity, 86.7% specificity, and 93.3% accuracy, in a cohort of ovarian cancer patients where normalization of CA125 had occurred after the surgery and completion of chemotherapy. One of those biomarkers was a peptide epitope from a known para neoplastic antigen, HARS. Para neoplastic antigens can elicit a humoral immune response in cancer patients as these antigens are expressed in the cells of nervous system and tumor. The appearance of these onconeural antibodies in ovarian cancer patients leads to the development of various neurological disorders called paraneoplastic syndromes, particularly dermatomyositis or polymyositis but can precede the occurrence of dermatomyositis or polymyositis. Although the clinical implication of these onconeural antibodies as biomarkers for early diagnosis of ovarian cancer has been reported in many case studies, the usefulness of these antibodies has yet to be evaluated in monitoring disease status in ovarian cancer patients after cytoreductive surgery and chemotherapy treatments.

The appearance of these onconeural antibodies in ovarian cancer patients leads to the development of various neurological disorders called paraneoplastic syndromes, particularly dermatomyositis or polymyositis but can precede the occurrence of dermatomyositis or polymyositis. Although the clinical implication of these onconeural antibodies as biomarkers for early diagnosis of ovarian cancer has been reported in many case studies, the usefulness of these antibodies has yet to be evaluated in monitoring disease status in ovarian cancer patients after cytoreductive surgery and chemotherapy treatments. Cancer is a highly heterogeneous disease and mutations that occur in genes and vary patient to patient. Further, recent studies using deep sequencing technology reveal that tumor tissue exhibit high degree of intratumoral heterogeneity harboring multiple clonal populations with the tumor. Therefore, the use of established cell lines as therapeutic vaccines may not represent all the clonal populations and will not be efficacious. Our laboratory has pioneered the development of a therapeutic cancer vaccine design that uses Tumor Membrane Vesicles (TMVs) prepared from tumor tissue and a novel protein transfer technology to adjuvant ate them. Using this approach it is feasible to develop cancer vaccines from surgically removed tumor tissues which incorporates all the antigenic variations found in the tissue. In this technology, immuno stimulatory molecules are attached to a glycolipid and then tethered to tumor membranes by a short-incubation, thus eliminating the need for gene transfer or live cells to develop cancer vaccines. The immuno stimulatory molecules incorporated onto tumor membranes serve as adjuvants to boost antitumor immunity against tumor-associated antigens expressed on cancer cell membranes. Experiments using mouse models of cancers have shown that membrane-based cancer vaccines prepared by protein transfer technology can protect mice from live tumor cell challenge suggesting that membrane-based cancer vaccines induce protective antitumor immunity.