CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180343

Project Title:
Turn ON the Tumor Contrast in Lymph Node Metastases for Occult Disease Detection

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Lymph node metastasis (LNM) is the most important determinant factor for survival for many solid cancers. The gold standard for detection of regional metastatic disease from most cancers is a regional nodal dissection and histologic examination by a trained pathologist. This can result in significant morbidity including shoulder dysfunction and pain in head and neck patients, and lymphedema, pain and impaired arm use in breast cancer patients. Sentinel lymph node biopsy is an alternative surgical staging method. However, small but significant false negative rates limit its clinical use. The objective of this application is to establish pH threshold sensors to detect occult lymph node metastasis in preclinical animal models. Dysregulated pH is a hallmark of malignant cancers as a result of the deregulated energetics. Malignant tumors have acidic tumor environment. Recently, our lab has established ultra-pH sensitive nanosensors that greatly amplified the tumor acidosis signals and allowed microscopic delineation of tumor margins. Real-time, fluorescence-guided surgery significantly improved the long-term survival in tumor-bearing mice over white light surgery. In this study, we will transform the optical detection method to a non-invasive positron emission tomography (PET) paradigm. Preliminary data has shown successful detection of orthotopic head and neck HN5 tumors with small size (~20 mm3, or <4 mm in diameter). PET imaging using an FDA-approved tracer, 2-deoxy-2-[18F]fluoroglucose (FDG) did not show cancer-specific detection of similar sized HN5 tumors but demonstrated significant accumulation in normal tissues leading to false positive results. This research will help establish the pH threshold nanosensor technology to identify occult lymph node metastases. We anticipate successful execution of this research will lead to a new paradigm that allows accurate staging of cancer nodal status in cancer patients for selective therapy with improved survival outcomes.