Defining the Role of Tumor-Secreted Exosomes in Lymph Node Metastasis

Principal Investigator:

- David C. Lyden, MD, PhD, Weill Cornell Medical College

Co-Principal Investigator:

- Babak Mehrara, MD, Memorial Sloan Kettering Cancer Center

Abstract: Metastasis is the most devastating phase of tumor progression in all cancers as commonly observed in melanoma. In solid cancers, lymph nodes are the most important indicator for clinical outcome and metastasis. Except for sarcomas, the majority of solid cancers metastasize from the primary tumor to the sentinel lymph nodes. Recent findings of microvesicle-based information transfer processes by exosomes promise to revolutionize our understanding of tumor progression. Melanoma-secreted exosomes have been shown to home to lymph nodes supporting metastatic progression. However, the molecular mechanisms underlying have not been exploited. We postulate that tumor-secreted exosomes promote changes in the lymph node microenvironment fostering metastasis. The goal of the current project is to determine the mechanisms through which tumor-derived exosomes promote lymph node metastasis and develop a state-of-the-art technology to predict lymph node metastasis. We propose to determine whether exosome cargo in the lymphatic fluid can be used as novel indicators of metastatic burden in melanoma. We will dissect the biological distribution of exosomes in the lymph and the role of specific pathways in tumor lymphangiogenesis and metastatic spread mediated through exosomes using mouse models, lymphatic fluid from melanoma patients, 3D models, assymetric flow fractionation and near infrared imaging techniques. Our studies in melanoma patients will be the first to evaluate the use of circulating vesicles in lymphatic fluid and define novel markers in negative sentinel lymph nodes to predict relapse and metastasis.