June 28, 11 am

« Plateforme Génomique Fonctionnelle » Campus Carrère,
University Bordeaux

An unanticipated role of the lymphatic vascular system in promoting distant organ metastasis

Michael Detmar, M.D., Professor of Pharmacogenomics, Institute of Pharmaceutical Sciences, ETH Zurich, Zurich, Switzerland

Previous studies by our laboratory and others have established the concept that tumor-induced lymphangiogenesis promotes cancer metastasis to lymph nodes. Tumor draining lymphatic vessels and the expanded lymphatic vessels in tumor-draining lymph nodes provide a (pre)metastatic niche for cancer stem cells, as evidenced by the occurrence of in-transit metastases and persistence of cancer cells in lymph node sinuses, mediated by specific chemokines. Using near-infrared in vivo imaging, we found enhanced flow in tumor-associated lymphatic vessels, as well as re-routing of lymphatic tumor drainage after sentinel lymph node metastasis. Evaluation of tumor-draining lymph nodes by light-sheet microscopy revealed that expansion of lymph node lymphatics precedes tumor metastasis, and transcriptional profiling of tumor-activated lymphatic vessels identified upregulation of factors involved in the control of the immune response such as PD-L1 and in tumor cell adhesion such as VCAM-1. Indeed, we found that lymphatic endothelium-expressed PD-L1 dampens anti-tumor immune responses. Our recent data indicate that lymphangiogenesis also occurs in distant organ metastases in human and experimental murine cancers, and studies in a genetic mouse model for increased lymphatic vessel density in the lung revealed that increased lymphatic density in peripheral organs promotes further cancer spread to other organs. Importantly, our studies also revealed that lymphangiogenesis in lung metastases of human cutaneous melanomas is correlated with lung-draining lymph node metastasis and with reduced overall patient survival. These findings reveal an unanticipated role of lymphatic vessels in facilitating systemic cancer metastasis.