Editorial

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Nodal status is the most important prognosticator for the outcome of cancer patients. Within the regional nodal basin, the sentinel lymph node is, in general, the first lymph node that will receive cancer cells from the anatomic site draining to this regional nodal basin. In about 20 % of the cases, systemic metastasis may occur without nodal involvement. The molecular mechanisms of lymphatic versus vascular spread still remain to be defined. In this special issue, Biomarkers in Cancer Metastasis through the Lymphovascular System, attempts are made to address the biomarkers and molecular mechanisms of cancer metastasis from the primary site to the distant sites by way of the lymphovascular system. This issue captures the presentations of the 4th International Symposium on Cancer Metastasis and the Lymphovascular System: Basis for Rational Therapy, which was held in New York City from May 12 to 14, 2011. Biomarkers in relationship to informatics are defined by Yu Shyr. Systematic and evidence-based discovery of biomarkers at the NCI is summarized by Sudhir Srivastava et al. Molecular profiling for personalized cancer care is emphasized by Raheela Ashfaq. Biomarkers for tumor progression in the tumor microenvironment relating to the heterogeneity of the tumor vasculature are described by Janice Nagy and Harold Dvorak. Stromal biomarkers in breast cancer development and progression are characterized by Jenny Rudnick and Charlotte Kuperwasser. Sentinel lymph node as a biomarker for gateway of metastasis is brought to light by

several important papers. First, a novel agent, Tilmanocept, has been found to be an excellent radiotracer to localize the prostate sentinel lymph node both in a canine model by David Vera et al. and in identifying breast cancer sentinel lymph nodes by Anne Wallace et al. Second, the role of breast cancer sentinel lymph nodes has been defined by the American College of Surgeons Oncology Group Z0011, that provokes a debate whether axillary lymph node dissection should be done for a positive sentinel lymph node biopsy in breast cancer by Armando Giuliano, Monica Morrow, Shivani Duggal and Thomas Julian. Third, the controversial role of sentinel lymph node in head and neck carcinoma is debated by Robert Ferris and Dennis Kraus. Fourth, the mature clinical trial results of melanoma sentinel lymph node are summarized by Donald Morton. From the clinical applications of sentinel lymph nodes, biological questions regarding cancer metastasis arise. First, Marlys Witte et al. attempt to establish the relationship between biomarkers, pathways, processes and syndromes in lymphatic development, growth and neoplasia. Second, lymphatics, lymph nodes and the immune system: barriers and gateways for cancer spread are addressed by Robert Ferris et al. Third, the connectivity of lymphogenous and hematogenous tumor cell dissemination: biological insights and clinical implications are brought to focus by Jonathan Sleeman et al. Fourth, Kelly Huynh and Dave Hoon introduces the concept of epigenetic molecules for regional lymph node metastasis. Fifth, as an exception to the rule in solid cancer that sarcoma rarely metastasizes through the lymph nodes, Elisabetta Pennacchioli et al. summarize the biomarkers of sarcoma and the patterns of metastasis. In the clinical arena, using melanoma as a clinical model, Stanley Leong et al. trace the progression of melanoma from the primary site to advanced stage IV disease with respect to the biomarkers of melanoma during its evolution

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and treatment at different stages of melanoma. Using circulating regulatory T cells as biomarkers, Nicola Mozzillo and Paolo Ascierto document the effect of high-dose interferon on these regulatory T cells in melanoma patients. Alison Stopeck et al. summarize the role of targeted therapy using biomarkers in breast cancer treatment. Harold Wanebo et al. address the biologic challenge of colorectal metastasis. By targeting oncogene-defined subsets of melanoma patients, Keith Flaherty presents the latest promising results from clinical trials on the effect of BRAF inhibitors for melanoma patients with mutant BRAF gene. Using monoclonal antibodies against cancer biomarker targets, Alain Pecking et al. identify the cancer targets using immuno-SPECT/CT and immuno-PET/CT. With relevant cancer biomarkers at hand, Dino Stea demonstrates the utility of targeted radiotherapy. Thus, the 4th International Symposium has addressed the significance of biomarkers in identifying cancer at its inception, progression and metastasis through the lymphovascular system.

The symposium has brought the basic scientists, radiologists and clinicians together resulting in cross fertilization between these disciplines in a translational approach to understand cancer metastasis. The symposium was able to link the bench to the bedside and vice versa.

Cancer progression from the primary site to the regional nodes and distant sites is an orderly process and is genetically controlled. In general, the sentinel lymph node is the gateway through which the cancer cells may metastasize beyond the nodal basin to distant sites. Cancer heterogeneity results in different subgroups of cancer patients, who may be selectively identified by genetic profiling with specific biomarkers so that more rational therapy can be tailored to different subgroups of patients. Gene profiles and specific biomarkers can be used to separate different subgroups of cancer patients and form the basis of correlative studies relating to cancer clinical trials. Thus, more targeted and personalized therapy may be delivered to cancer patients.