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EDITORIAL

Editorial

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The 7th International Cancer Metastasis Symposium through the Lymphovascular System: Biology & Treatment, was held from April 20–22, 2017 in San Francisco, California. This international conference was inaugurated in 2005 and has been successfully held biennially with several publications summarizing the biology and treatment of cancer metastasis [1–5]. The 7th International Cancer Metastasis Symposium in April 2017 in San Francisco brought together international experts in oncology, immunobiology, pharmacology, molecular biology and molecular imaging to discuss preclinical, translational and clinical advances in diagnosing, treating and preventing cancer metastasis [5].

The theme of the Symposium is to follow the primary cancer growth in our body resulting from cellular mutations. These mutant cells proliferate within the cancer microenvironment, which like the Darwinian selective force [6–9] allows the development of the "fittest" clone to spread through the lymphovascular system from the primary site. The cancer cells with the ability to metastasize tend to go through the sentinel lymph node first in about 80% of the time, which may serve as a primary gateway or incubator for the cells to proliferate or spread to distant sites to cause devastation to the body. It is a journey that needs to be understood from a molecular level so that the mutant cells can be stopped before they go awry.

We want to thank our sponsors and exhibitors who have made this Symposium a success. Each of them is acknowledged and listed in our website [5].

We are indebted to the Editorial Board of the Clinical and Experimental Metastasis to allow us to publish the presentations of the 7th International Cancer Metastasis Symposium in this special issue with most of the presentations being included. We are grateful to all the presenters and authors, who have summarized their presentations as review articles being published in this special issue. In addition to the plenary session presentations, the Symposium was enhanced by special topics relating to the central theme of cancer metastasis and being presented as mini-symposia in the breakfast and lunch sessions.

Charles Balch reviews the clinical utility of sentinel lymph nodes as he delivered the Donald L. Morton Surgical Oncology Memorial Lecture. Stanley Leong, Atena Aktipis and Carlo Maley emphasize the importance of cancer microenvironment as it relates to cancer initiation and progression. Michael Dellinger and Marlys Witte address the mechanisms of cancer metastasis. Jacob Ankeny, Brian Labade, Jason Luke, Eddy Hsueh, Jane Messina and Jonathan Zager examine the prognostic utility of biomarkers in malignant melanoma. Noel Turner, Olivia Ware and Marcus Bosenberg present the latest development in genomics as an important arena to study cancer metastasis. Isaac Witz et al. describe the molecular interaction between melanoma cells and brain microenvironment resulting in the development of melanoma brain metastasis. Diego Marzese, Ayla Manughian-Peter, Javier Orozco and David Hoon explore the epigenetic alterations of spliceosome factors being associated with melanoma metastasis. Using the model of melanoma metastatic to the sentinel lymph nodes, Mark Faries, Dale Han, Michael Reintgen, Lauren Kerivan, Douglas Reintgen and Corrado Carraco develop the concept of melanoma sentinel lymph node as an incubator versus a marker for early melanoma metastasis and the significance of melanoma sentinel lymph node as a staging tool and its application in subgrouping melanoma patients. David Nathanson, David Krag, Henry Kuerer, Lisa Newman, Markus Brown, Dontscho Kerjaschki, Ethel Pereira and Timothy Padera update the biology and treatment of breast cancer metastasis to the regional lymph nodes and beyond. Stanley Leong, Bernard Fox, Mojca Skoberne and others project novel frontiers to study cancer microenvironment using multiplex microscopy, neoantigens as targets for immunotherapy against cancer, microRNA and circulating tumor cells as

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potential biomarkers for cancer metastasis. Evan Weitman and Jonathan Zager summarize the latest treatment for in-transit metastatic melanoma. Thein Swe and Kevin Kim update the promising treatment modalities using targeted therapy and check point inhibitors for melanoma and other types of cancer. John Chan et al. share with us the exciting therapeutic developments in the gynecological cancers. Russell Witte describes the latest novel modalities in cancer imaging. Borrowing from the concept of melanoma and breast cancer sentinel lymph node, Sukamal Saha, Markus Zuber, David Wiese, and others demonstrate the importance of micrometastasis of colon cancer sentinel lymph node as a biomarker for adjuvant therapy. Hiroya Takeuchi and Yuko Kitagawa update on the indications and results of sentinel lymph node mapping in upper gastrointestinal cancer. Further, Timothy Wilson and Ramkishen Narayanan apply the sentinel lymph node concept in the study of prostate cancer sentinel lymph nodes. Russell Witte describes the latest novel modalities in cancer imaging. As an important modality in the treatment of primary and isolated metastatic cancer by radiation therapy, Dino Stea, Roy Abendroth and Charles Hsu summarize the new frontiers of radiotherapy against cancer. As lymphedema is a significant complication from cancer treatment such as surgery and radiotherapy, Michael Bernas, Saskia Thiadens, Betty Smoot, Jane Armer, Paula Stewart and Jay Granzow address the issues relating to lymphedema following cancer therapy. Separately, Jay Granzow describes the different surgical options for the treatment of lymphedema.

Thus, the above-mentioned reviewed articles were organized to bring forth that cancer cells, through cellular mutations, proliferate within the cancer microenvironment, which exerts a selective force to allow the development of aggressive clones to initiate the process of metastasis. In most of the time, the sentinel lymph node is the primary gateway to the distant sites. Occasionally, the cancer cells may bypass the sentinel lymph nodes throught the vascular system. The immune system may be critical in its interaction with the cancer cells both in the primary and metastatic site. With rapid development of molecular and genomic techniques, the molecular mechanisms of cancer metastastasis via the lymphatic versus vacular routes or both will be further defined. Sentinel lymh node biology and concept formulate the central theme of cancer metastasis in the current sentinel lymph node era as appropriately reflected in the publication of this special issue. Cancer progression from the primary site to the regional nodes and distant sites is an orderly and genetically controlled process. The American Joint Committee on Cancer, currently at its 8th edition [10], has aptly captured this process according to the Tumor, Node and Metastasis (TNM) characteristics extracted from evidence-based publications and cancer databases relating to the pathologic and clinical correlation with respect to the disease-free and overall survival of cancer patients. Molecular and genomic data of cancer patients are rapidly emerging. In the future, these important biomarkers may be incorporated into the clinical TNM system to enhance its accuracy and enable better subgrouping of cancer patients. Perhaps, molecular taxonomy may be established in addition to the TNM system so that cancer patients can be better staged to receive more effective personalized treatments.

As cancer biology is being advanced rapidly in the laboratory, we become more aware that cancer mutation is the basis of cancer heterogeneity. Both the host microenvironment and therapeutic modalities serve as "natural selection" forces, a term being borrowed from Darwin [9], which may select out the "fittest clone" among the many heterogeneous clones within the cancer population to spread beyond the primary site. Therefore, it is critical to understand the molecular relationship between cancer growth and its microenvironment as well as the host influence such as the immune system with its complexity in cancer progression. Perhaps, there is a unifying concept of cancer mutation, initiation, progression and metastasis on a molecular basis. With more detailed understanding of the genomic and molecular characteristics of cancer, we are closer towards the practice of precision medicine with tailored approaches to individual patient or groups of patients. It is our plan to address these issues in detail in our upcoming 8th International Cancer Metastasis Congress to be held in San Francisco from October 25–27, 2019 [5] with the goal to bring basic scientists, oncologists, surgeons and radiologists from around the world together to allow cross-fertilization of ideas resulting in the translation of basic science into clinical application and challenging basic scientists with clinical issues. We hope that with advancements in cancer biology, treatment and care, caner survivors may live longer and enjoy an improved qualtiy of life than before.

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