OVER 14 MILLION CANCER CASES were diagnosed worldwide in 2012, and cancer incidence is expected to increase in the coming years (3, 9). The rising numbers of cancer survivors in many countries makes the identification of new therapeutic options an increasingly pressing issue (5). Tumor recurrence and metastasis is the most frequent cause of morbidity and mortality in cancer survivors and thus need to be a focus for new therapeutic developments. A central issue in the treatment of metastatic cancers is that these tumors gain resistance to chemotherapeutic and targeted biological agents (2, 4, 7). Despite the healthcare and economic burdens associated with cancer recurrence, many aspects of the basic biology and physiology of tumor metastasis remain poorly understood. Many open questions remain about the triggers or predispositions that lead to early invasion of cancer cells away from the primary tumor, or that then favor intravasation or long-term survival of tumor cells in secondary organs.

This series of AJP-Cell Physiology Reviews highlights recent research that is yielding insights into the early events that can promote metastatic disease. Metastasis initiation is considered to involve cancer stem-like cells with long-term self-renewal capability, which are often under high selection pressure and may exhibit the ability to transition between migratory and proliferative states (6). It is increasingly recognized that the local microenvironment, including extracellular matrix and normal cell types of the tumor-adjacent stroma, has an important role in determining cancer cell behaviors. In addition, evidence for preconditioning of metastatic niches by secreted or exosomal products of the cancer cells themselves has highlighted the complexity of the dialogue that occurs between cancer and stromal cells (1).

Much of the research in these areas relates to breast or colon carcinomas, which are among the most common forms of cancer worldwide. However, there are rarer cancers with very poor survival rates. A prime example is ovarian cancer, in which the mechanisms that drive dissemination within the peritoneal cavity appear to be very different from those that underlie tumor invasion within a solid tissue. We open this series with a Review by Samuel C. Mok (M.D. Anderson Cancer Center) and colleagues on the current knowledge of cellular and molecular mechanisms of ovarian cancer metastasis (10). The issue also features a Review by Rajender K. Motiani (CSIR-Institute of Genomics and Integrative Biology) and colleagues on the dysregulation of STIM and Orai proteins in many cancers and the possibility of targeting these proteins as a form of cancer therapy (8). Future Reviews in this Theme will include articles that provide perspectives on the nature of tumor-initiating cells, mechanisms that enable cancer cells to enter the blood circulation, and the molecular basis of communications between tumor cells and the extracellular matrix and microenvironment in distant organs.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS
J.C.A. and T.O. drafted, edited, revised, and approved the final version of this manuscript.

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