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Cell and Molecular Processes in Cancer Metastasis: An AJP-Cell Physiology set of Themed Reviews

Josephine C. Adams[1], Thordur Oskarsson[2]

[1] School of Biochemistry, University of Bristol, Bristol BS8 1TD, UK
Email: jo.adams@bristol.ac.uk

[2] Heidelberg Institute for Stem Cell Technology and Experimental Medicine (HI-STEM gGmbH) and German Cancer Research Center (DKFZ), Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany
Email: t.oskarsson@dkfz-heidelberg.de

Over 14 million cancer cases were diagnosed worldwide in 2012 and cancer incidence is expected to increase in the coming years[1,2]. The rising numbers of cancer survivors in many countries makes the identification of new therapeutic options an increasingly pressing issue[3]. Tumor recurrence and metastasis is the most frequent cause of morbidity and mortality in cancer patients and thus needs 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[4-6]. 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 pre-dispositions 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, that are often under high selection pressure and may exhibit the ability to transition between migratory and proliferative states[7]. It is increasingly recognised 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 pre-conditioning 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[7,8].

Much of the research in these areas relates to breast or colon carcinomas, that are amongst 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 Mok (M.D. Anderson Cancer Center) and colleagues on the current knowledge of cellular and molecular mechanisms of ovarian cancer metastasis[9]. The issue also features a Review by Rajender 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[10]. 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.

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