AJP-Cell Physiology begins a Theme on "Cellular Processes in Tumour Metastasis - From Basic Research to Translation"

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Cancers are so life-threatening not so much because of the ability of cancerous tumors to develop rapidly as by the risk of the spreading of tumor cells out of their originatation site. This proces is called metastasis. The term "metastasis" was proposed in 1829 in the context of cancer by Joseph Claude Recamier, a French physician who was the first to report anatomical observations in his book entitled “Recherche sur le traitement du cancer” that showed that the metastases came from the emigration of cancer cells out of the primary (breast) tumor and of their transplant into organs distant from the home of the primary cancer (5).

Metastases cause 90% of the patient mortality due to malignant carcinomas. Unfortunately, it should be noted that the prognosis of a patient with metastatic cancer is not much better now than it was ten or twenty years ago. Indeed, many patients, at the time of diagnosis, already have occult metastases (also known as micrometastases). These render the surgical or radiotherapeutic action ineffective, since it these treatments eradicate only the primary tumor and leave in place the secondary tumors. Later these may develop and current chemotherapeutic treatments are rarely effective. This explains the urgency to find new type(s) of chemotherapy targeted at metastatic disease and the need to better understand the biological mechanisms that are implemented during metastatic progression.

It is known that cancer cells can migrate locally into nearby non-tumoural tissue parenchyma, they can also spread to lymph nodes, tissues as well as to distant parts of the body. The cellular and molecular characteristics of metastatic cancer cells are somehow similar to those of the initial tumour cells but in the process of metastasis they are selected for their capacity to cope with non-native and stressful environments (6). Indeed, most of the time, spreading cancer cells die at some point in this process, but some of them are capable to form new tumors in other parts of the body and thus display the fittest and most adapted phenotype. Metastatic cancer cells can also remain inactive/dormant at a distant site for many years before they grow again, if at all (2). Carcinoma cells spread through the body in a series of steps. These steps include i) the growth into, or invasion, nearby non-tumoural tissue; ii) the capacity to slide through the walls of nearby lymph nodes or blood vessels, this process is called intravasation; iii) the ability of metastatic cells to travel through the lymphatic system or bloodstream to other parts of the body, this process is called circulation of the tumor cells; iv) adhesion to small blood vessels at a distant location and invasion of the blood vessel walls, this process is called extravasation; v) the formation of premetastatic lesions into the surrounding tissue, and formation of micrometastases; vi) colonization of the tissue and formation of new blood vessels to allow the metastatic tumor to grow (7). All these processes involve aberrant cell communication mechanisms that can be mediated at each stage by exposure of select proteins at the tumor cell surface (e.g. adhesion molecules), by the production of soluble materials (e.g. growth factors or chemokines), or by extracellular vesicles (3).

These aberrant cell communication mechanisms together with tumor cell intrinsic gain-of-functions (e.g. endoplasmic reticulum stress (4)) provide metastatic tumor cells with specific features that allow them to exert specific effects on neighboring cells in the tissue of origin, to evade the immune system, circulate in the blood stream and colonize the distant tissue. The first Review in this series addresses the roles of exosomes in metastatic tumour cell communications (3). The understanding and the characterization of the molecular mechanisms activated to drive metastasis will not only allow the identification of potential biomarkers that may predict at an early stage for instance the presence of premetastatic lesions but also lead to the design of novel effective therapeutics (1), thereby demonstrating the relevance of such translational approach.

We thank the authors for their excellent Reviews and believe that readers will find the Review articles in this Theme of interest. In addition, we hope that the ideas and results provided in the articles will stimulate experiments that address unanswered questions regarding cellular and molecular mechanisms controlling metastasis that may assist translational efforts to make tumour metastasis a non-life-threatening condition. look forward to receiving original manuscripts in response to the accompanying Call for Papers on “Cellular Processes in Tumour Metastasis - From Basic Research to Translation” which will start in October 2019.

Disclosures

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