Escaping from, moving towards, following a path, squeezing through: lots of opportunities for moving cells

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Eukaryotic cells move within the surrounding environment essentially for two reasons: the necessity to reach a predetermined site or the hostility of the primitive site. Moving in the direction of an attractive site or factor is typical for embryonic movements and metastatic dissemination of cancer cells and motility strategies are very similar for both categories. Activation of an epigenetic process called epithelial mesenchymal transition (EMT) is indeed characteristic of embryonic development, of fibrotic or regeneration processes, and of the spreading of cancer cells from their primitive origin [1,2]. The most aggressive cancers have developed a further program of cellular plasticity that is very useful to adapt to particular environmental changes, i.e. the mesenchymal amoeboid transition (MAT). This additional strategy is associated with the deregulation of important oncosuppressor pathways and the hyperexpression of oncogenes, especially those linked to the activation of the Rho GTPase family [3]. The choice of migration styles enables cells to use ad hoc mesenchymal or amoeboid modes of motility and grants to cells of aggressive cancers the ability to move in environments with different structural characteristics using either matrix proteases to degrade the extracellular matrix (ECM) or squeezing between its gaps. This adaptability of motility styles to the environment is currently considered to be the main reason for the failure of clinical trials testing protease inhibitors in patients with metastatic cancers. Brabek et al. [4] review in this special issue the role of matrix stiffness and composition for plasticity of cancer cell motility, while Parri and Chiarugi [5] focus on the role of Rho GTPases for the ad hoc switch between different motility strategies.

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The nervous system also plays an important role in cell motility, for two reasons: the secretion of neurotransmitters which also act as motility factors and the contribution of an alternative escaping way to migrating cells, commonly called perineural invasion. In this special issue Voss and Entschladen review this aspect with a particular focus on the role of catecholamine and stress mediators on tumoral cell motility [13].

As mentioned at the beginning, a second reason for cells to move is the escape from an hostile ambiente, for example due to the scarcity of growth factors (chemotaxis), due to the presence of improper ECM (aptotaxis and durotaxis), because of the accumulation of toxic or pro-oxidant factors (escaping from primitive tumoral or inflammatory sites) or to escape oxygen or nutrient deprivation (hypoxia and ischemia). De Donatis et al. [14] focus their review on the role of growth factor gradients as regulators of a motile phenotype in which cells aim to reach a definite growth factor concentration that is suitable for cell duplication. In this context, the motile and proliferative phenotypes are mutually exclusive and the review of De Donatis et al. clarifies the role of growth factor receptor clustering and internalization in the choice between migration and duplication. While chemotaxis and durotaxis are detailed by Brabek et al. [4], the role of a pro-oxidant and/or low oxygen environment in the regulation of cell motility has been recently reviewed by Pani and Chiarugi [15].

Far from being exhaustive, this special issue focused on cell motility aims to underscore the fertility of the current research efforts in this field, as well as highlighting key questions that still are awaiting definitive answers.

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