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Introduction: Cell invasion: cooperation between gene families at distinct levels

J. Heino[a,b] and V.-M. Kähäri[a,c]

[a]MediCity Research Laboratory, Department of Medical Biochemistry, University of Turku, FIN-20520 Turku (Finland)
[b]Department of Biological and Environmental Science, University of Jyväskylä, FIN-40351 Jyväskylä (Finland)
[c]Department of Dermatology, Turku University Central Hospital, FIN 20520 Turku (Finland)

In intact tissues, cells are surrounded by extracellular matrix (ECM) and any cell movement requires penetration through a meshwork of connective tissue molecules. In addition, more organized structures of the ECM, such as basement membranes, form molecular barriers that prevent movement of cells from one compartment to another. However, in certain conditions, cell movement through basement membranes is required. Recent findings in cell biology have revealed the complex molecular interactions underlying cell movement in physiological phenomena such as lymphocyte trafficking, embryonic tissue development, tissue repair, and hormone-dependent tissue turnover. Elucidating the basic mechanisms of cell movement has also greatly benefited cancer biology, as the invasion of tumor cells into the surrounding tissue and subsequent formation of metastases are the most important reasons for cancer mortality.

The cellular mechanism of invasion is based on a molecular network consisting of several families of proteins. It is obvious that the cell adhesion apparatus plays a central role in this phenomenon. Adhesion receptors, especially the integrins, anchor cells to the ECM and are needed in the formation of new contacts between the cell and the matrix proteins essential for movement. Integrins are connected to the cytoskeleton, including the actin-containing microfilaments. Cell movement requires constant remodeling of microfilaments and the small GTPases are maybe the most important group of signaling proteins regulating this process. Integrin signaling connects the GTPases to the same network. Cell invasion requires proteolytic activity and degradation of ECM components. The families of matrix metalloproteinases (MMPs) and serine proteinases can degrade components of the ECM, including fibrillar collagens, basement membrane molecules, connective tissue glycoproteins, and proteoglycans. The balance between these proteinases and their physiological inhibitors, such as the tissue inhibitors of metalloproteinases, is critical in cell invasion.

The multi-author review published in this issue contains six papers which shed light on different aspects of cell invasion. The two first papers give an overview on the MMPs (Johansson et al.) and the integrins (Ivaska and Heino) and summarize the present knowledge about their role in cell migration and invasion. Recent information indicates that the two families interact and may regulate invasion together rather than separately. Andreasen et al. review a third important family of proteins, serine proteases, that can easily be placed in the same molecular network with integrins and MMPs. Friedl and Böcker describe the use of three-dimensional matrix in the research on cell locomotion. Their observations provide new insights into cell movement in tissues and help to put the other observations in the right context. Some of the most interesting new observations in invasion research indicate the role of GTPases in the regulation of actin organization. This field is reviewed by Hernandez-Alcoceba et al. Finally, the paper by Fata et al. focuses on the hormone-dependent remodeling of ECM in ovary, uterus, and mammary tissue, and provides an example of the importance of cell movement and invasion in physiological processes.

Current knowledge about cell invasion is based on research on ECM structure, deposition and proteolysis, cell adhesion, cell signaling, and cytoskeleton

organization. Complex interactions between the molecules involved in these processes make cell locomotion possible, and to understand cell invasion we must understand the cross-talk between these distinct groups of proteins. Given the importance of cell movement in the progression of cancer and in various physiological situations, it is likely that the basic research on molecular mechanisms of invasion will lead to important applications in the treatment of human diseases.

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