THE EXTRACELLULAR MATRIX

Role of the Extracellular Matrix

The microenvironment plays an important role in defining the roles of localized cells. A major component of that microenvironment is the Extracellular Matrix (ECM), a reservoir of macromolecules that provide signaling cues to cells to attach, proliferate, differentiate, vascularize and become a functional tissue.

Through direct or indirect means the ECM regulates almost all cellular behavior and is indispensable for major developmental processes.

ECM Signaling Cues include:

1. integrin attachment ligands
2. cytoskeletal anchors
3. soluble growth factors
4. remodeling enzymes
5. homing receptors
6. differentiation markers

The Extracellular Matrix: A dynamic niche in cancer progression (Pengfei Lu, Valerie M. Weaver, and Zena Werb)

"The local microenvironment, or niche, of a cancer cell plays important roles in cancer development. A major component of the niche is the extracellular matrix (ECM), a complex network of macromolecules with distinctive physical, biochemical, and biomechanical properties. Although tightly controlled during embryonic development and organ homeostasis, the ECM is commonly deregulated and becomes disorganized in diseases such as cancer. Abnormal ECM affects cancer progression by directly promoting cellular transformation and metastasis. Importantly, however, ECM anomalies also deregulate behavior of stromal cells, facilitate tumor-associated angiogenesis and inflammation, and thus lead to generation of a tumorigenic microenvironment. Understanding how ECM composition and topography are maintained and how their deregulation influences cancer progression may help develop new therapeutic interventions by targeting the tumor niche.

"Much effort has been devoted to determining how cellular components of the niche initiate and promote cancer development (Bhowmick et al., 2004). However, recent progress has also highlighted the importance of noncellular components of the niche, especially the ECM, during cancer progression (Sternlicht et al., 1999; Paszek et al., 2005; Erler et al., 2006, 2009; Levental et al., 2009). Although long viewed as a stable structure that plays a mainly supportive role in maintaining tissue morphology, the ECM is an essential part of the milieu of a cell that is surprisingly dynamic and versatile and influences fundamental aspects of cell biology (Hynes, 2009). Through direct or indirect means, the ECM regulates almost all cellular behavior and is indispensable for major developmental processes (Wiseman et al., 2003; Stickens et al., 2004; Rebustini et al., 2009; Lu et al., 2011)."[1]

[1]Source: Pengfei Lu,[1,2,3,4,5] Valerie M. Weaver,[6] and Zena Werb[4,5] "The extracellular matrix: A dynamic niche in cancer progression." The Rockefeller University Press J. Cell Biol. Vol. 196 No. 4 395–406 www.jcb.org/cgi/doi/10.1083/jcb.201102147.

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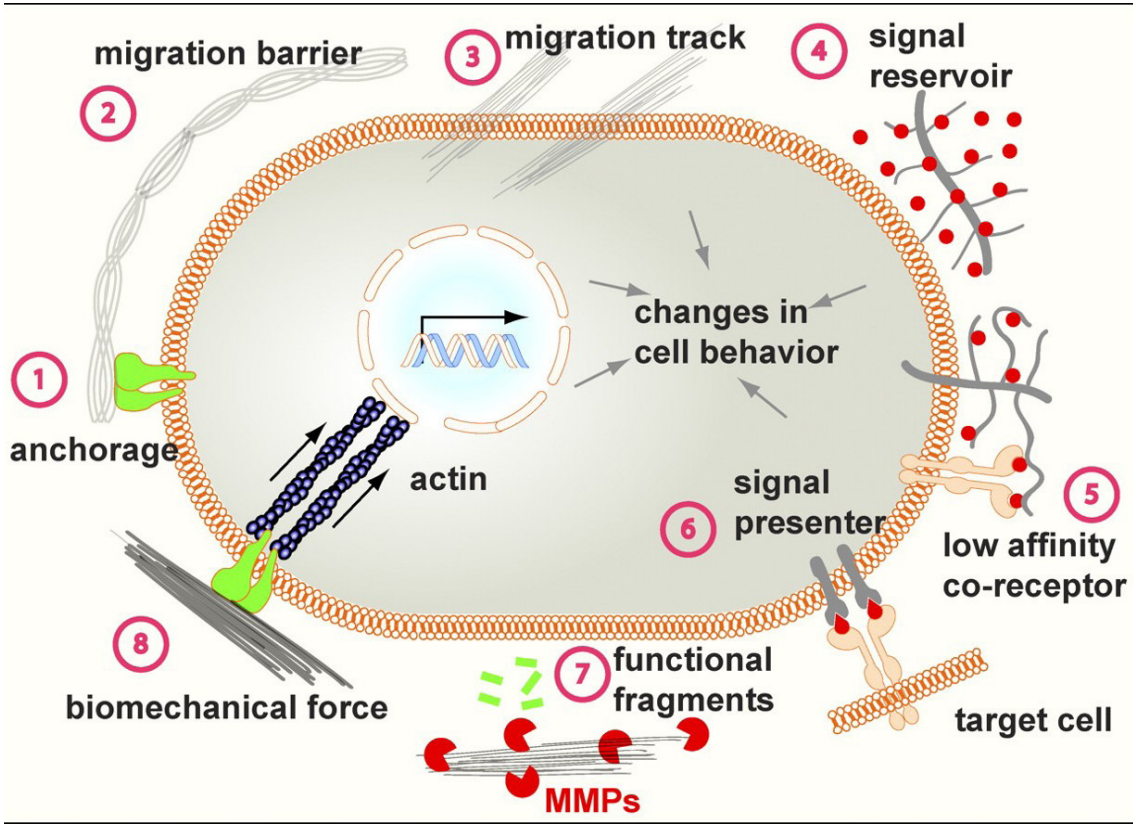
Mechanisms of ECM Function

"The versatile functions of the ECM depend on its diverse physical, biochemical, and biomechanical properties. Anchorage to the basement membrane is essential for various biological processes, including asymmetric cell division in stem cell biology and maintenance of tissue polarity (stage 1). Depending on contexts, the ECM may serve to block or facilitate cell migration (stages 2 and 3). In addition, by binding to growth factor signaling molecules and preventing their otherwise free diffusion, the ECM acts as a sink for these signals and helps shape a concentration gradient (stage 4). Certain ECM components, including heparan sulfate proteoglycans and the hyaluronic acid receptor CD44, can selectively bind to different growth factors and function as a signal coreceptor (stage 5) or a presenter (stage 6) and help determine the direction of cell–cell communication (Lu et al., 2011). The ECM also direct signals to the cell by using its endogenous growth factor domains (not depicted) or functional fragment derivatives after being processed by proteases such as MMPs (stage 7). Finally, cells directly sense the biomechanical properties of the ECM, including its stiffness, and change a wide variety of behaviors accordingly (stage 8)."[1]



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