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Journal club

THE MATRIX REVOLUTIONS

The extracellular matrix (ECM), the complexity of which once rendered it an ugly stepchild of cell biology, is undergoing another renaissance. Originally recognized as the glue that holds tissues together, it became apparent in the 1960s that the ECM also dictates cellular behaviour; for example, it was shown that muscle cells require collagen for differentiation. Emerman *et al.* and Lee *et al.* extended this observation by showing that hormone-induced differentiation of mammary epithelial cells was enhanced by releasing the collagen gel on which they were growing from the substratum (collagen release had previously been shown to promote liver differentiation). Cellular contraction accompanied this release, and collagen crosslinking inhibited differentiation, suggesting that contraction and pliability regulate epithelial gene expression. Adhesion and pliability are now known to influence the behaviour of other differentiating cell types, with integrin-mediated adhesions sensing and relaying the pliability information.

> “pliability directs mesenchymal stem cell lineage specification.”

A few years ago, McBeath *et al.* and Engler *et al.* reignited interest in the field by demonstrating that pliability directs mesenchymal stem cell lineage specification. Highly pliable ECMs produce neurons, rigid ECMs produce bone and ECMs with intermediate pliability produce muscle. Although the pliability is interpreted by myosin II activity, the interplay between force and adhesive signalling that dictates the resulting cellular response remains to be understood.

These studies have enormous ramifications. Stem cell therapy requires transplanted cells to migrate, proliferate and differentiate appropriately in response to the chemical and physical environment. Similarly, the tumour microenvironment can dictate the behaviour of tumour and stromal cells through its effect on adhesive signalling, which can influence the efficiency of therapy. Thus, increasing our understanding of microenvironments, and the mechanisms by which adhesive signals are sensed and transduced into cellular responses, may have important clinical implications.

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