Metastatic movements in 3-D

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Caswell et al.report in the *Journal of Cell Biology* how the altered behavior of integrins can prompt metastatic movement in tumor cells.

On 2D surfaces, cells may migrate randomly, or be strongly unidirectional. Integrins, which link the cell to the extracellular matrix, are known to influence the mode of migration, but exactly how has been unclear.

Recent work has suggested that an integrin called a5b1 drives random movement, while an integrin called avb3 has been associated with unidirectional migration—the balance of activity between the two determining the type of movement. To further explore the contribution of a5b1 to random migration, the authors thus blocked avb3.

The treated cells changed their mode of migration from unidirectional to random, and their ability to invade 3D gels increased. The changed behavior correlated with an increase in trafficking of a5b1 from intracellular compartments to anterior membrane protrusions. But this increase in trafficking did not significantly alter a5b1's contribution to cell adhesion—the ease with which cells were dislodged from a spinning disk increased as the amount of avb3 was reduced, but was not correlated with any change in a5b1. This suggested that the cells' increased invasive ability was due to alteration in some other property. That property turned out to be activation of a proinvasive pathway headed by a kinase called Akt.

In avb3-blocked cells, a5b1 became associated with epidermal growth

factor receptor 1 (EGFR1), which increased EGFR1's abundance at the membrane protrusions, as well as its autophosphorylation. Because EGFR1 is an activator of the Akt pathway, hey presto, the cells took on some new moves.

Source: Rockefeller University Press