**Protrusion provides a prognosis**

How a cancer cell migrates across a 2D surface says little about its ability to move through a 3D matrix, Meyer et al. reveal, but measuring membrane protrusion can be much more informative.

A metastasizing tumor cell moves through 3D tissues, yet, largely because they’re easier to perform, most studies of cell migration are carried out on 2D surfaces. Meyer et al. wanted to investigate how well 2D assays replicate 3D motility and to determine what parameters best predict a cell’s migration through 3D environments.

The researchers tracked the migration of several breast cancer cell lines on a variety of 2D and 3D matrices in response to different growth factors associated with metastasis. The speed and directional persistence of the cells’ movements on 2D surfaces bore little resemblance to their behavior in 3D matrices. And, although a cell’s migratory response to different growth factors could be partially predicted by measuring which growth factor receptors it expressed, differences in receptor expression and activation levels couldn’t account for all the variation seen in different cell lines.

Meyer et al. then examined whether any individual steps of 2D migration correlated with 3D motility and found that the extent to which cells formed membrane protrusions in response to different growth factors was a reliable predictor of their 3D migratory behavior. Strengthening the connection, cytoskeletal inhibitors that preferentially block 3D migration also impeded membrane protrusion in 2D. The authors now want to develop high-throughput methods for measuring membrane protrusion in order to facilitate screens for drugs and siRNAs that affect 3D cell migration.

Meyer, A.S., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201201003.

**The ribosome runs a systems test**

The ribosome runs a systems test

**IFT-A goes both ways**

The intraflagellar transport A (IFT-A) complex regulates Sonic hedgehog (Shh) signaling by trafficking membrane proteins into primary cilia, Liem et al. reveal. Vertebrate cells require a primary cilium to activate Shh signaling because many of the pathway’s key components accumulate inside these microtubule-based organelles. Primary cilia themselves rely on two multi-subunit transport complexes, IFT-A and IFT-B. IFT-B moves proteins to the tips of cilia, and, in the absence of the complex, cells are unable to form cilia or activate the Shh pathway. IFT-A’s main role, on the other hand, has been thought to be the recycling of proteins out of the primary cilium. Mice lacking certain IFT-A subunits have swollen primary cilia and show ectopic Shh activity.

Liem et al. identified two mouse lines with different mutations in the IFT-A subunit *ift144*. One line, named *twinkletoes*, expressed a weakly active version of IFT144 and was similar to other IFT-A mutant mice in having slightly larger primary cilia and enhanced Shh signaling. The *diamondhead* line, however, produced no IFT144 protein, had very short cilia, and showed a decrease in Shh activity. This suggests that, in addition to its recycling function, IFT-A transports proteins into cilia and, like IFT-B, is required for cilia assembly. Indeed, several membrane-associated components of the Shh pathway were missing from the short cilia of *diamondhead* mice. Soluble pathway components were still present in cilia, however, perhaps indicating a division of labor between IFT-A and IFT-B.

Shh activity may be increased in *twinkletoes* mice because less adenyl cyclase is transported into their primary cilia. The researchers propose that this membrane-associated enzyme normally generates cyclic AMP in order to activate protein kinase A, a potent inhibitor of the Shh pathway.

Liem, K.F., Jr., et al. 2012. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201110049.