Skeleton key for cancer metastasis

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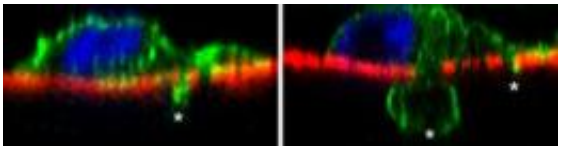

An actin-rich invadopodium pushes through the basement membrane (red, left), allowing the tumor cell to follow (right). Credit: Schoumacher, M., et al. 2010. J. Cell Biol. doi:10.1083/jcb.200909113.

Cancer cells need all three of their cytoskeletons—actin, microtubules, and intermediate filaments—to metastasize, according to a study published online on April 26 in the *Journal of Cell Biology*.

A cancer cell in an epithelial layer is trapped unless it can force through the basement membrane, which cordons off the tissue. Tumor cells start to dissolve the basement membrane with enzymes that build up within extensions called invadopodia. How the different components of the cytoskeleton collaborate to spring the cell remains unclear. To find out, Danijela Vignjevic and colleagues (Institut Curie) followed cancer cells as they started their breakout.

They found that a tumor cell escapes in three stages. First, stumpy protrusions dig into the basement membrane. These structures then elongate into "mature" invadopodia. Finally, the rest of the cell follows. In culture, crawling cells produce extensions that carry either bundles of actin or an actin mesh. In the cancer cells, both forms of actin were

necessary for invadopodia to form and grow. However, microtubules and intermediate filaments were only essential for invadopodia to lengthen.

The researchers suggest a model for this initial step of metastasis. Growing actin bundles push out a protrusion, which the actin mesh stabilizes as it elongates. Only if the invadopodium stretches beyond 5 microns do microtubules and intermediate filaments get involved. Microtubules most likely elongate the invadopodium by delivering materials such as enzymes to the tip. Intermediate filaments, meanwhile, may brace the growing extension.

More information: Schoumacher, M., et al. 2010. J. Cell Biol. doi:10.1083/jcb.200909113

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