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CELL MIGRATION

Putting pressure on the lead

Multiple modes of migration are available to cells, depending on cell type and the physical properties of the environment. Whereas lamellipodia-driven, actomyosin-dependent cell migration has been well studied on two-dimensional (2D) extracellular matrices (ECMs), less is known about the lamellipodia-independent mechanisms of cell migration that can occur in more physiological 3D environments. For example, fibroblasts migrating through a linearly elastic 3D ECM are characterized by blunt cylindrical protrusions known as lobopodia. Petrie and colleagues describe how the nucleus functions as a piston to pressurize the cytoplasm at the leading edge of a migrating cell to generate these lobopodia.

They showed that intracellular hydrostatic pressure was significantly increased in lobopodial cells migrating in a 3D cell-derived matrix compared with lamellipodial cells migrating in 2D or in a 3D nonlinearly elastic ECM. Furthermore, the hydrostatic pressure was compartmentalized in lobopodial, but not lamellipodial, cells with the nucleus separating a high-pressure anterior compartment from a lower-pressure posterior compartment. The nucleus physically divided the cytoplasm of these cells and was observed to be pulled forward periodically in the cell away from the trailing edge. Inhibiting actomyosin contractility in front of the nucleus but not behind it prevented forward pulling of the nucleus, equilibrated the pressure across the cell, decreased the overall hydrostatic pressure and ultimately switched cells to lamellipodial migration. The authors conclude that actomyosin-dependent forward motion of the nucleus pressurizes the anterior cytoplasmic compartment to enable lobopodial protrusion.

A complex of actomyosin, vimentin and nesprin 3 was immunoprecipitated from lobopodial cells. Nesprin 3 is a nucleoskeleton–cytoskeleton linker protein that is thought to transmit force from actomyosin to the nucleus. In line with this, in nesprin 3 siRNA-treated lobopodial cells, the nucleus lost the ability to move independently of the trailing edge such that anterior and posterior intracellular pressures were reduced and equalized. This resulted in the loss of anterior lobopodial protrusions, a switch to lamellipodia and decreased cell velocity.

So widely divergent mechanisms of cell migration can be used by cells according to their physical environment, with individual cells being able to switch between migration modes.

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ORIGINAL RESEARCH PAPER Petrie, R. J., Koo, H. & Yamada, K. M. Generation of compartmentalized pressure by a nuclear piston governs cell motility in a 3D matrix. *Science* **345**, 1062–1065 (2014)