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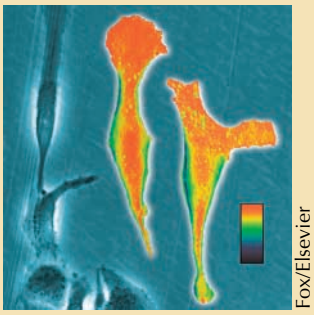

Fox/Elsevier

Leading edges have stiffer edges (red).

Inflexibility in motion

Cell migration depends on polarized actin polymerization at a cell's front edge. To get the most out of these actin networks, plasma membrane flexibility must be similarly polarized, according to results from Amit Vasanji, Paul Fox (Cleveland Clinic Foundation, Cleveland, OH), and colleagues.

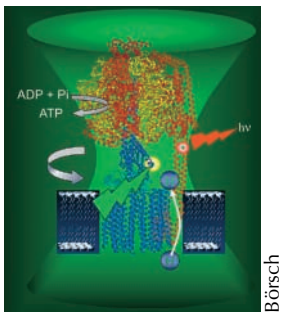
The group shows that the membrane is stiffest at the front of migrating endothelial cells. This oriented flexibility is fine-tuned through cholesterol distribution. Growth factors that induce migration in vascular cells caused cholesterol to concentrate at the leading edge, and this gradient was needed for migration. In liposomes, addition of a modest amount of cholesterol (thus creating a stiffer membrane) promoted the ability of actin to deform the membrane.

One might expect a flexible membrane to be more easily moved by polymerizing actin, but Fox compares actin in a cholesterol-free cell to a finger pressed into a balloon. "It's so flexible," he says, "a filament gets completely surrounded. There's no room for more monomers to come in. With some stiffness, [a filament] pushes forward a section [of membrane] that leaves room for more actin." The effect may be compounded by the exclusion of bundling and cross-linking proteins. This theory is supported by the authors' findings that growth factors stabilize the forward actin network. The group next hopes to determine how growth factors orient cholesterol trafficking, possibly through transport proteins such as caveolin-1. ■

Reference: Vasanji, A., et al. 2004. *Dev. Cell.* 6:29–41.

Winding and unwinding ATP synthase

Like a revolving door, bacterial ATP synthase turns two ways, according to Manuel Diez, Michael Börsch (Universität Stuttgart, Germany), and colleagues. One direction makes ATP, whereas the other breaks it down.



Börsch

ATP synthase turns one way to make ATP and the other to break it down.

ATP synthase is a two-component nanomotor. One part of the enzyme (F_0) lies within the lipid bilayer and translocates protons across the membrane, whereas the other (F_1) makes or breaks ATP. Recent studies have shown that each portion contains a subunit that turns within the rest of the protein framework, thus giving ATP synthase a reputation as a rotor. F_1 rotation had been best shown during ATP hydrolysis, because the microscopy methods used needed soluble protein, but the enzyme requires a proton gradient across a membrane to make ATP.

To solve this problem, the German group used fluorescence resonance energy transfer to study the protein within liposomes, thus allowing them to create a proton gradient. In ATP synthesis mode, the enzyme adopted three sequential positions—similar to the 120° steps seen during hydrolysis with microscopy methods. However, the direction of rotation was opposite to that of hydrolysis. F_0 is thought to rotate smoothly during proton translocation, so researchers next need to determine how that is translated to discrete steps in F_1. Börsch also wonders how cellular conditions toggle the switch from synthesis to hydrolysis and back again. ■

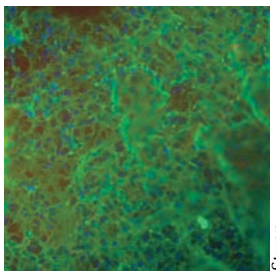
Reference: Diez, M., et al. 2004. *Nat. Struct. Biol.* 11:135–141.

Nanofibers have the right stuff

Tiny fibers designed by Gabriel Silva, Catherine Czeisler, John Kessler, Samuel Stupp, and colleagues (Northwestern University, Chicago, IL) provide stem cells the environment they need to make clinically desired cells. Although the researchers produced neurons, the design is amenable to many cell types.

The group has created a peptide nanofiber solution that assembles into three-dimensional networks when it contacts biological fluids. On the face of the resulting scaffold sits a laminin-derived epitope that directs neurite growth. In vitro, neural progenitors cells (NPCs) encapsulated by the scaffold differentiated into neurons. On laminin, in contrast, fewer and smaller neurons formed, and some NPCs formed astrocytes.

Astrocytes are thought to be a major obstacle in recovery from paralysis after spinal cord injury, so the nanofibers may speed healing in ways our own physiology cannot. "The [epitope] density [in the scaffold] is a thousand times higher than you would have if you packed [laminin] into a crystal and the epitopes were exposed on the surface," says Stupp. "Somehow, this abiotic presentation causes cell differentiation to change."


Stupp

Nanofibers with the right epitope support neurons (green) but not astrocytes (red).

The fibers also assemble when injected in vivo. Although the experiments are still in progress, rats with spinal cord injuries seem to heal faster when treated with the nanofiber solution. With the right epitope, the nanofibers can be modified to support growth of bone, blood vessels, islet cells for diabetic patients, and other cells. ■

Reference: Silva, G.A., et al. 2004. *Science.* 10.1126/science.1093783.