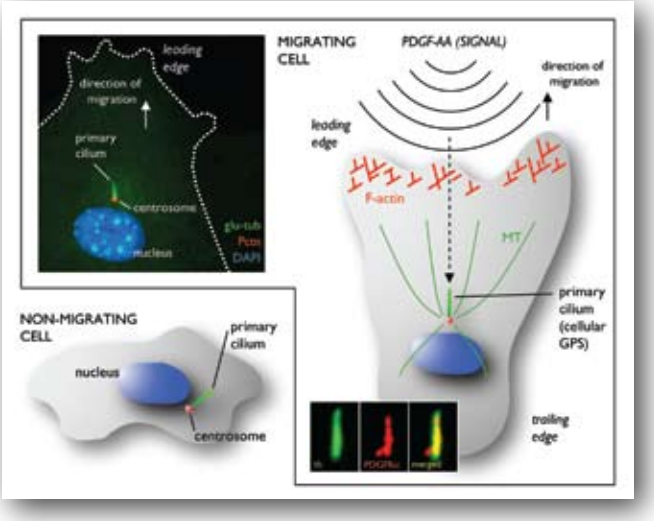
Steering aid

The primary cilium serves as a "cellular GPS" in wound repair and beyond

If cells held high school reunions, the primary cilium would be the class nerd who comes back in glory as a bioscience millionaire. Once written off as a vestigial organelle left in the evolutionary dust, the primary cilium has in the last decade risen to prominence as a vital cellular sensor at the root of everything from polycystic kidney disease to cancer to left–right anatomical abnormalities. Now comes evidence that the primary cilium may act as a "cellular GPS," orienting cells that play a critical role in wound healing to move in the right direction.



The primary cilium (upper left) functions as a cellular GPS to coordinate directional cell migrating. PDGF-AA is a chemo-attractant (upper right) that signals through its receptor, PDGFRa, in the fibroblast cilium, which then orients in front of the nucleus and parallel to the migration path. Signaling through the cilium causes reorganization of cytoskeletal components (F-actin and microtubules, MT), leading to directional cell migration. The fluorescent image (inset in upper left) shows a migrating cell with the cilium stained with anti-detyrosinated tubulin (glu-tub, *green),* the centrosome with pericentrin (Pctn, *red)* and the nucleus with DAPI (*blue).* The inset images (bottom right) show that PDGFRa (*red*) localizes to the cilium stained with anti-acetylated tubulin (tb, *green).*

Soren T. Christensen and colleagues at the University of Copenhagen in Denmark and the Albert Einstein College of Medicine in the Bronx have discovered that the primary cilia of cultured fibroblasts are oriented to detect a growth factor signal critical to efficient wound closure. When properly stimulated, the primary cilia steer fibroblast cells toward the wound. Furthermore, mice with engineered defects in the formation of primary cilia show a reduced rate of wound repair and have defects in wound closure.

"The really important discovery is that the primary cilium detects signals, which tell the cells to engage their compass reading and move in the right direction to close the wound," Christensen explains. The primary cilia are solitary, antenna-like structures that protrude through the membrane from a centrosome at the cell surface. Primary cilia are found on almost every nondividing cell in the body. "In mutant cells that lack the [primary] cilium," Christensen continues, "cell migration is unregulated with uncontrolled directional cell displacement during wound closure, leaving the cells blindfolded to some of the signals that permit the cells to navigate correctly."

The primary cilium uniquely carries a critical receptor for platelet-derived growth factor alpha (PDGFR-α). When activated by its ligand, PDGF-AA, PDGFR-α transmits information from the cilium to the cell, reorganizing the cellular cytoskeleton and causing it to move the cell in the right direction and at a faster pace. This mechanism is blocked in mutant cells with no primary cilia. "What we are dealing with is a physiological analogy to a global positioning system with a coupled autopilot that coordinates air traffic or tankers on the open sea," says Christensen.

The researchers suspect that this cellular GPS plays other roles beyond wound healing. They say that it could serve as a fail-safe device against uncontrolled cell movement. Without chemical stimulation, the primary cilium would restrain cell migration, preventing the dangerous displacement of cells that is associated with invasive cancers and fibrosis. On the other hand, a defective primary cilium might fail to provide correct directional instructions during cell differentiation. The researchers suggest that this could be another factor linking the primary cilium to severe developmental disorders.

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The Primary Cilium Coordinates Directional Cell Migration

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