# Primary cilium as cellular 'GPS system' crucial to wound repair

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The primary cilium, the solitary, antenna-like structure that studs the outer surfaces of virtually all human cells, orient cells to move in the right direction and at the speed needed to heal wounds, much like a Global Positioning System helps ships navigate to their destinations.

"What we are dealing with is a physiological analogy to the GPS system with a coupled autopilot that coordinates air traffic or tankers on open sea," says Soren T. Christensen, describing his recent research findings on the primary cilium, the GPS-like cell structure, at the American Society for Cell Biology (ASCB) 48th Annual Meeting, Dec. 13-17, 2008 in San Francisco.

Christensen and his colleagues at the University of Copenhagen in Denmark and the Albert Einstein School of Medicine in the Bronx studied the primary cilia in lab cultures of mice fibroblasts, the cells that along with related connective tissues sculpt the bulk of the mammalian body.

They discovered that these cilia are oriented to detect a growth factor critical to the efficient repair of wounds. When properly stimulated by the protein factor, the primary cilia steered fibroblast cells toward the wound. If the primary cilia were genetically engineered to be defective, wound repair did not occur as quickly. In addition, the closure of wounds was incomplete in the mice with defective cilia, compared to rodents with normal cilia.

"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.

"In mutant cells that lack the primary cilium," Christensen says, "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 protein signal that activates the primary cilia is the platelet-derived growth factor (PDGF-AA), the ligand for platelet-derived growth factor (PDGFR alpha). The scientists found that when the primary cilia contain unique receptors for PDGFR alpha and that when turned on by the ligand, the receptors transmitted information from the cilia to the cell that resulted in the reorganization of the cellular cytoskeleton. The reorganization signaled the cells to move in the right direction and pace. This process did not occur in mutant cells with no primary cilia.

The researchers suspect this cellular GPS system plays roles other than wound healing. The primary cilia could serve as a fail-safe device against uncontrolled cell movement, says Christensen. Without chemical stimulation, the primary cilia would restrain cell migration, preventing the dangerous displacement of cells that is associated with invasive cancers and fibrosis, the scientists explain. On the other hand, defective primary cilia might fail to provide correct directional instructions during cell differentiation. This failure could be another link connecting primary cilia to severe developmental disorders, the researchers suggest.

Protruding through the cell membrane, primary cilia occur on almost every non-dividing cell in the body. Once written off as a vestigial organelle discarded in the evolutionary dust, primary cilia in the last decade have risen to prominence as a vital cellular sensor at the root of a wide range of health disorders, from polycystic kidney disease to cancer

to left-right anatomical abnormalities.

Source: American Society for Cell Biology