

Cilia: small organelles, big decisions

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Johns Hopkins researchers say they have figured out how human and all animal cells tune in to a key signal, one that literally transmits the instructions that shape their final bodies. It turns out the cells assemble their own little radio antenna on their surfaces to help them relay the proper signal to the developmental proteins “listening” on the inside of the cell.

The transmitters are primary cilia, relatively rigid, hairlike “tails” that respond to specialized signals from a host of proteins, including a key family of proteins known as Wnts. The Wnts in turn trigger a cascade of shape-making decisions that guide cells to take specific shapes, like curved eyelid cells or vibrating hair cells in the ear, and even make sure that arms and legs emerge at the right spots.

“Our experiments go to the heart of the development and maintenance of our body tissue,” says Johns Hopkins geneticist Nicholas Katsanis, Ph.D., associate professor at the McKusick-Nathans Institute for Genetic Medicine. “Any miscues with the Wnt signaling pathway,” says Katsanis, “and you’re looking at major childhood diseases and defects.”

In a report published on September 30 in *Nature Genetics*, Katsanis and his team used a small transparent fish, zebrafish, to literally watch what happened if they chemically blocked the production of three proteins that are required for primary cilia function during the period when a fish egg develops into a grown up, fully-finned fish.

The more they blocked, the more developmental errors - for example,

the growing fish would not properly extend their tails - they were able to track to defective Wnt signaling.

Katsanis notes that once inside a cell, the Wnt pathway splits into two branches that need to be balanced depending on the needs of each cell: the so-called canonical branch, which typically drives cells to multiply, and the non-canonical branch, which controls messages to refine cell shape and growth. The errors seen in the fish pointed to an imbalance where canonical signaling predominated.

A series of biochemical studies revealed that cilia normally help a cell keep the right balance by selectively destroying proteins in the canonical branch to prevent excess growth. Defective ciliary function therefore leads to defective destruction of key proteins, which then causes problems in interpreting the Wnt signal.

“We thought that the key to the balancing act occurred inside the cell, but it now seems clear that the cilia are the main relay stations,” Katsanis says. “We’ve just reset a huge volume of literature under a new light.”

Source: Johns Hopkins

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