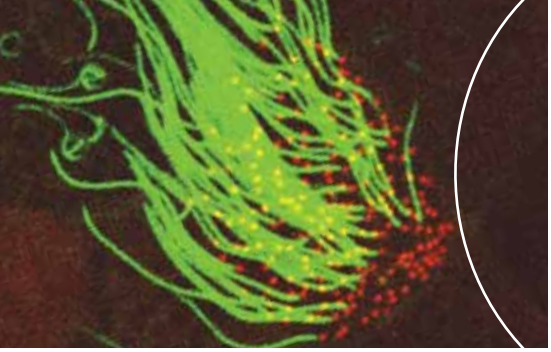

Christopher R. Kintner

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"We are studying the genetic and developmental mechanisms that guide the formation of ciliated cells, with the goal of using this information to better diagnose and treat ciliopathies, which can cause respiratory problems, middle ear infection, and infertility."

Tiny hairlike structures called motile cilia sweep mucus and dirt out of our lungs, propel the egg from the ovary through the Fallopian tube into the uterus, and move fluid through the brain's ventricles. A lot is known about the structural details of cilia: An array of microtubules arranged in nine doublets around a central pair is anchored through the so-called basal body inside the cell. But how cilia form in epithelial cells and how they coordinate the direction of their stroke along a common polar plane is far from clear.

The Kintner lab has identified the gene FoxJ1 as a key factor required for motile cilia, but on its own, FoxJ1 can only induce the formation of a single cilium. By searching for genes that are only expressed in cells that make hundreds of motile cilia, Kintner and his team identified a novel gene, called multicilin. When expressed in nonciliated cells, it both activates FoxJ1 and a program required to form hundreds of basal bodies, resulting in multiciliated cells that are indistinguishable from those found in the lung. Ongoing studies are elucidating the genetic mechanisms that allow multicilin to convert epithelial cells into multiciliated cells.

In a separate study, Kintner's group tracked the orientation of hundreds of cilia in Xenopus frog larvae, whose skin is covered with multiciliated cells. They found that during early embryonic development, cilia point more or less in the general direction of the body's back end and start creating a weak flow. During the following refinement phase, all cilia get in line and trim their sails to the prevailing winds. When they analyzed the planar cell polarity (PCP) pathway, which is widely used as a mechanism to orient structures within cells and tissues, they found that the PCP pathway has several functions in ciliated cells: It not only orients cilia in a specific planar direction through cell–cell interactions but also positions basal bodies within cells so that cilia can form.

Identifying the components involved in cilia-specific functions and in the molecular mechanisms underlying the various ciliopathies is likely to facilitate the development of novel therapeutic strategies.

For more information, please visit
salk.edu/faculty/kintner.html

Left to right:
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