# Gene mutation leads to poorly understood birth defects

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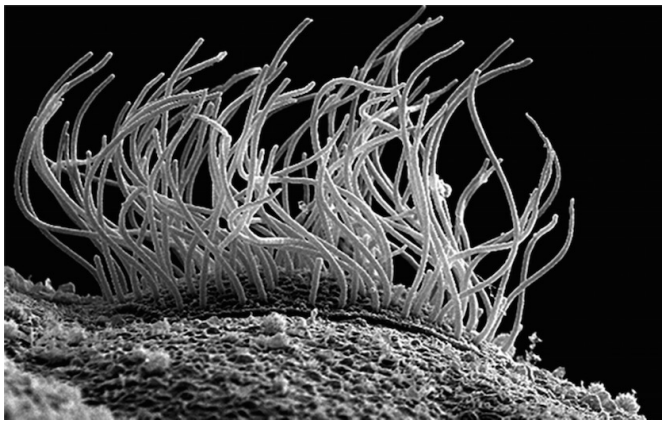

Cilia. Credit: John Wallingford

Scientists have identified genetic mutations that appear to be a key culprit behind a suite of birth defects called ciliopathies, which affect an estimated 1 in 1,000 births. In a paper published online this week in *Nature Genetics*, a team of researchers led by The University of Texas at Austin's John Wallingford reveals that these mutations prevent certain proteins from working together to smooth the way for cells to communicate with one another.

Birth defects from genetic disorders of the cilia—tentacle-like structures in cells that coordinate cell-to-cell communication in healthy people—are varied, ranging from oral-facial-digital syndrome, which can cause extra toes, misshapen teeth, an abnormal tongue and other defects, to short rib polydactyly syndrome, a lethal birth defect that causes every organ in the body to be defective.

"For cells to talk to each other, functioning cilia are needed," says Wallingford, a professor in the Department of Molecular Biosciences. "We identified a group of proteins that form part of the base that cilia need in order to function. If that base is defective, it can cause serious birth defects that are frequently lethal."

The new research pinpoints how three proteins work together to form a base that allows cilia to carry critical cell-to-cell communications. Wallingford and his colleagues discovered that, much the way that cellphone towers provide a base for the antennas that assist with communication, these proteins together construct a base that anchors the cilia. Disturbances in the little-known group of proteins, which the researchers called CPLANE, led to disturbed cell communication and observable ciliopathy in mouse models. The team also asked human geneticists to screen for the genes among their patients with similar birth defects and found that mutations in the same genes resulted in ciliopathies in humans.

Wallingford points out that the research is important, given that ciliopathies are more widespread than most people realize. Polycystic kidney disease, for example, which causes the abnormal growth of cysts on kidneys, is a disorder arising from defective cilia and afflicts about 600,000 people in the U.S.

"If you lump ciliopathies, the prevalence is high, and they will become one of the more common congenital diseases," says Wallingford. "Birth defects are an underappreciated problem, and we have little understanding of their genetic underpinnings despite their prevalence, not to mention their environmental underpinnings."

**More information:** Michinori Toriyama et al, The ciliopathy-associated CPLANE proteins direct basal body recruitment of intraflagellar transport machinery, *Nature Genetics* (2016). DOI: 10.1038/ng.3558

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