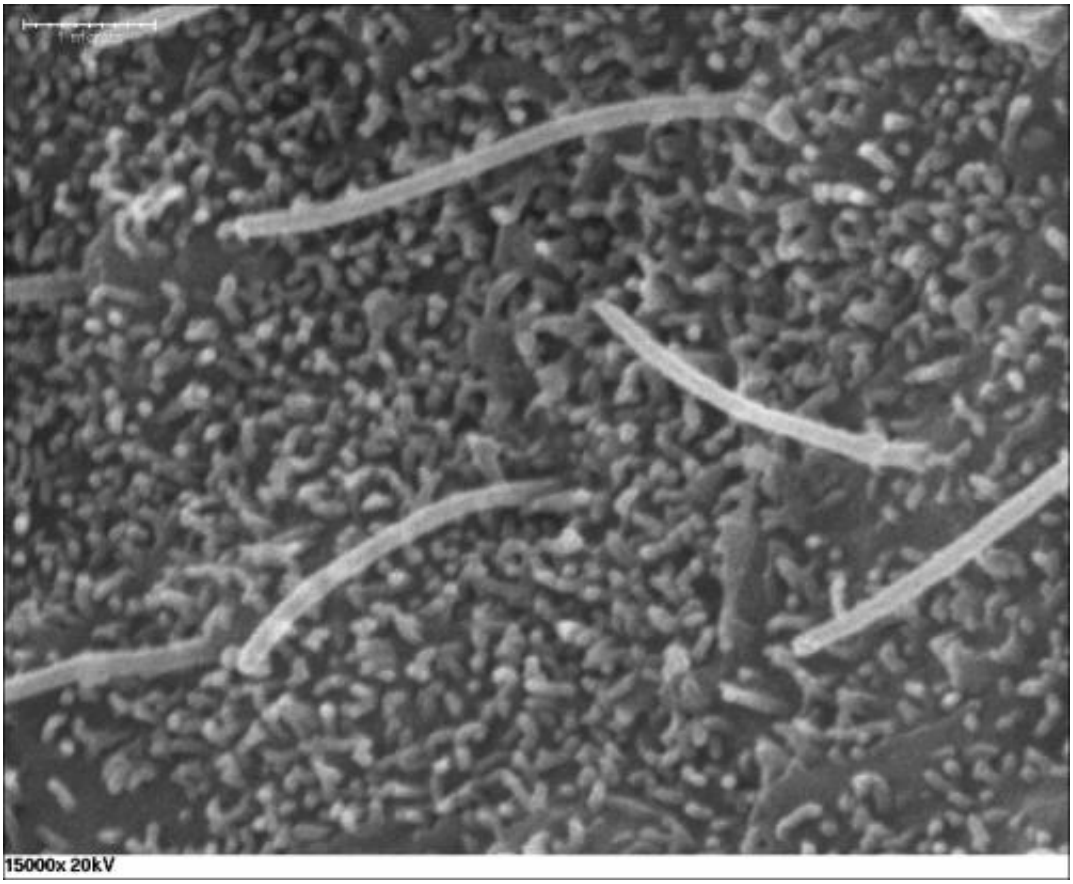
Critical protein discovered for healthy cell growth in mammals

January 27 2014, by Krista Weidner



Using mouse models, Penn State cellular biologist Aimin Liu and his colleagues discovered a protein that is required for the growth of critical, hair-like structures called cilia on cell surfaces. The cilia on a mouse embryo, shown in this micrograph, would not be able to grow without the protein C2cd3. Credit: Aimin Liu lab, Penn State University

(Phys.org) —A team of researchers from Penn State University and the University of California has discovered a protein that is required for the growth of tiny, but critical, hair-like structures called cilia on cell surfaces. The discovery has important implications for human health because lack of cilia can lead to serious diseases such as polycystic kidney disease, blindness and neurological disorders.

"If we want to better understand and treat diseases related to cilium development, we need to identify important regulators of cilium growth and learn how those regulators function," said co-author Aimin Liu, associate professor of biology at Penn State. "This work gives us significant insight into one of the earliest steps in cilium formation."

The researchers describe their findings in a paper that will be published online in the *Proceedings of the National Academy of Sciences* during the week of 27 January 2014. In addition to Liu, authors include Penn State cellular biologists Xuan Ye, Huiqing Zeng and Gang Ning, as well as Jeremy F. Reiter, a biophysicist at the University of California - San Francisco.

Cilia, which are present on the surface of almost all mammalian cells, are responsible for sending, receiving, and processing information within the body. "You could think of cilia as the cells' antennae," Liu said. "Without cilia, the cells can't sense what's going on around them, and they can't communicate." Cilia also perform important filtering and cleansing functions. For example, cilia inside the trachea, or windpipe, trap and prevent bacteria from entering the lungs.

In a previous study, Liu and his colleagues learned that a protein called C2cd3 is important for cilium formation because mice that lacked this protein exhibited severe developmental problems typically associated with the lack of cilia. "At the time we knew only that if we get rid of the protein, the cells in the animal would not grow cilia," Liu said. "We

didn't understand why, but now we do."

A cilium grows from a centriole, a structure that clings to the inner surface of the cell and serves as an anchor for the cilium. Before a cell can grow a cilium, it needs to assemble a set of appendages at one end of the centriole. These appendages can then connect the centriole to the cell surface, allowing the outgrowth of a cilium. Just how these appendages are assembled, though, remained a mystery for more than four decades since their discovery in 1962. Liu and his colleagues found that appendages were not assembled at the end of the centriole when the C2cd3 protein is not present. As a result, the centriole is not associated with the cell membrane and cannot recruit other proteins for the further growth of the cilium. "So our protein is required for the very first step of putting a cilium together," Liu explained. "Without those appendages, the cilium growth cannot happen."

The researchers hope their discovery will lead to greater knowledge of the process of cilium development and, eventually, to treatments for a wide range of health problems that fall under the label of ciliopathy. "Ciliopathy is a scientific term that covers a lot of diseases," Liu said. As well as contributing to cystic disorders in the kidney and liver, lack of cilia can lead to blindness or deafness, since cilia in the retina serve as receptors that process light stimulation and cilia within the ear are required in neurons that translate sound waves into neural signals.

More information: C2cd3 is critical for centriolar distal appendage assembly and ciliary vesicle docking in mammals, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1318737111

Provided by Pennsylvania State University