# News Release

## Title

Mechanism of hydrocephalus development by *Daple* gene mutation

## Key Points

- Multiple motile cilia on the surface of the lateral ventricle guide the cerebrospinal fluid flow and the neuroblast migration by their coordinated beatings.
- We found that Daple is essential for the coordinated orientation of cilia whose abnormality leads to hydrocephalus.
- Our findings provide new insights into pathogenesis of hydrocephalus and respiratory diseases such as asthma


## Summary

Motile cilia in ependymal cells, which line the cerebral ventricles, exhibit a coordinated beating motion that drives directional cerebrospinal fluid flow and guides neuroblast migration. At the apical cortex of these multi-ciliated cells, asymmetric localization of planar cell polarity (PCP) proteins is required for the planar polarization of microtubule dynamics, which coordinates cilia orientation. Daple is a disheveled-associating protein, which controls the non-canonical Wnt signaling pathway and cell motility. Here, we show that Daple-deficient mice present hydrocephalus, and their ependymal cilia lack coordinated orientation. Daple regulated microtubule dynamics at the anterior side of ependymal cells, which in turn oriented cilial basal bodies required for the directional cerebrospinal fluid flow. These results demonstrate an important role for Daple in planar polarity in motile cilia and provide a framework for understanding the mechanisms and functions of planar polarization in the ependymal cells.


## Research Background

Motile cilia in ependymal cells, which line the cerebral ventricles, exhibit a coordinated beating motion that drives directional cerebrospinal fluid flow and guides neuroblast migration.

## Research Results

Mutations in human *DAPLE* were found in consanguineous families with autosomal recessive hydrocephalus. We demonstrated *Daple*-deficient mice present the lack of coordinated orientation of ependymal cilia and abnormal ependymal flow, leading to hydrocephalus.

## Research Summary and Future Perspective

These results demonstrate an important role for Daple in planar polarity in motile cilia and provide a framework for understanding the mechanisms and functions of planar polarization in the ependymal cells.

## Publication

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DOI：10.1016/j.celrep.2017.06.089

## Japanese ver.

https://www.med.nagoya-u.ac.jp/medical_J/research/pdf/Cell_R_20170726.pdf