Medical Xpress

Defective intercellular connections cause hydrocephalus

May 16 2017

About one in 2,000 babies are born with hydrocephalus, a condition in which cerebrospinal fluid (CSF) cannot flow towards the spinal column and builds up instead in the cavities (ventricles) of the brain. This causes the head to swell like a balloon and puts pressure on the brain. Various neurological symptoms can occur as a result including headache, vomiting, impaired vision, loss of coordination, seizures and cognitive difficulties. There are various causes of hydrocephalus. In some cases the condition is caused by a genetic abnormality.

The research team led by Andreas Fischer from the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) in Heidelberg already discovered in 2013 that a defect in a gene called Mpdz causes hydrocephalus in mice. In the same year, scientists from Saudi Arabia identified its human counterpart as a genetic cause of hydrocephalus in humans.

Now Fischer and his team have been able to uncover the mechanism underlying this genetic defect. The scientists observed in newborn mice with defective Mpdz that the ependyma, a cellular layer separating the brain nervous tissue from the CSF, is severely damaged. In order to maintain this vital dividing line, cells of a different type, called astroglia, fill in and ensure that the dividing tissue layer remains stable. However, this has a high price: Scar tissue develops in the ependyma leading to blockage of the so-called aqueduct, a channel connecting two ventricles of the brain, thus blocking the flow of cerebrospinal fluid.

"Evidence suggests that loss of the Mpdz gene reduces the stability of so-called tight junctions between adjacent ependymal cells, explains Anja Feldner, who is the first author of the study. The gene product of Mpdz controls molecules that play a crucial role for the stability of tight junctions. In fact, experiments in the Petri dish have shown that these junctions are impaired between ependymal cells with defective Mpdz. "This means we have uncovered a crucial mechanism that underlies the onset of genetic hydrocephalus," Fischer commented.

More information: Anja Feldner et al, Loss of Mpdz impairs ependymal cell integrity leading to perinatal-onset hydrocephalus in mice, *EMBO Molecular Medicine* (2017). DOI: 10.15252/emmm.201606430

Provided by German Cancer Research Center