Scientists pinpoint brain-swelling mechanism

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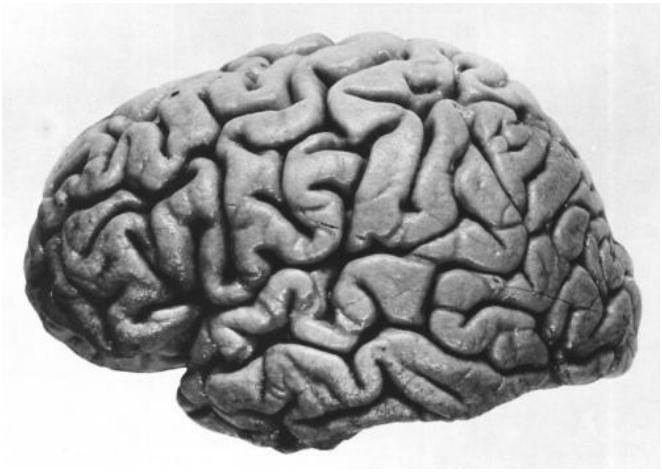

Left hemisphere of J. Pi?sudski's brain, lateral view. Credit: public domain

A team of UBC researchers has made a significant discovery uncovering the cause of brain swelling after trauma to the head. Their research, published today in *Cell*, paves the way for a preventative drug treatment for severe brain damage following stroke, infection, head injury or cardiac arrest.

By turning off a single gene, scientists from the Djavad Mowafaghian Centre for Brain Health (DMCBH), a partnership of UBC and Vancouver Coastal Health, were able to successfully stop swelling in rodent brains.

Brain swelling is a gradual process that becomes life-threatening within days of the injury, and is caused by sodium chloride drawing water into the nerve cells. This swelling—known as cytotoxic edema—eventually kills brain cells.

"We've known for years that sodium chloride accumulation in neurons is responsible for brain swelling, but now we know how it's getting into cells, and we have a target to stop it," explains brain researcher Brian MacVicar, co-director of DMCBH with the Vancouver Coastal Health Research Institute and the study's principal investigator.

The team, including Terrance Snutch, director of translational neuroscience at the DMCBH, developed several novel technological approaches to identify the cascade of events that took place within individual brain cells as they swelled.

They then switched off the expression of different genes and were able to pinpoint a single protein—SLC26A11—that acts as a channel for chloride to enter nerve cells. By turning off the chloride channel, the accumulation of fluid into the cells was halted, and nerve cells no longer died.

"It was quite a surprising result, because we had few indications as to what this protein did in the brain," says Ravi Rungta, then a graduate student in the MacVicar lab and the paper's lead author.

Though the technique used by the researchers to block swelling and cell death is unlikely to work quickly enough to mitigate swelling in the case of real head trauma, the discovery has provided a target for drug development.

"This discovery is significant because it gives us a specific target - now that we know what we're shooting at, we just need the ammunition," says MacVicar. "That's what we're doing now: looking for drugs to inhibit the chloride channel."

About brain swelling:

Severe brain swelling is life threatening because the skull, which normally protects the brain, also limits its ability to expand. With increasing pressure and nowhere to go, the brain centres that control breathing can be crushed.

At present, treatment options are limited. When all

other treatment options fail, an operation called a decompressive craniectomy is sometimes performed, in which a portion of the skull is removed and the brain is allowed to swell out of the skull. Although extreme, it can save the patient's life, but the procedure is not always effective nor without complications. There is an urgent need for new treatments.

Some well-known figures whose lives were claimed by brain injuries include actress Natasha Richardson (wife of actor Liam Neeson), who died in 2009 after a skiing accident and Dr. Richard Atkins, creator of the Atkins diet, who died in 2003 after slipping on ice.

Provided by University of British Columbia