Shutting off a gene causes mobility issues, researchers say

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Marek Michalak and Allison Kraus worked with an international team of medical researchers.

Researchers at the University of Alberta have discovered that shutting off an important gene in the body causes mobility issues, reminiscent of neurological diseases like multiple sclerosis.

The discovery may have major implications for neurological diseases and other disorders of the nervous system that deal with something called myelin impairment. Myelin is the protective coating around neurons and is important because it allows messages to quickly travel within the nervous system.

Two scientists from the Faculty of Medicine & Dentistry, Marek Michalak and Allison Kraus, made the discovery while working with an

international team of medical researchers, including colleagues throughout Alberta. About five years ago, Michalak and Kraus decided they wanted to research a specific type of gene that is responsible for the protein folding ability in cells. Depending on the protein and their purpose in a cell, they "fold" themselves into certain shapes to perform their function. They assemble themselves based on the instructions they get from genes in the cell. But i f protein-folding functions in cells don't work properly, it can lead to a host of diseases, including multiple sclerosis.

The duo wanted to specifically study what would happen if they removed a specific chaperone, a protein used in the cell-folding process, called calnexin. In doing so, they inadvertently created a neurological disease in their experimental models. The laboratory models had numerous mobility issues and the speed of messages being relayed in the nervous systems of the test subjects were delayed as well. The symptoms displayed were very similar to the symptoms seen in people with myelin impairment diseases such as MS and Charcot Marie Tooth disease, a neurological disorder that involves myelin impairment.

"It was a surprise," says Kraus, a PhD student. "We never expected to find out what we did. Then we needed to expand our study and that's when it became a bigger and more collaborative effort with numerous researchers around the globe becoming involved."

Michalak and Kraus say their findings provide a step forward in understanding the complexity of neurological diseases and may one day lead to the development of better treatments for common neurological diseases. The next step for researchers is to study DNA from people with certain neurological diseases to see if this gene contains mutations that could contribute to their disease.

The results of the duo's research, recently published in *The Journal of*

Biological Chemistry, clearly showed for the first time that chaperones impact myelin, something that no one had realized until now.

“Myelin diseases are so diverse and so tricky to figure out,” says Michalak, a professor in the department of biochemistry. “Nobody understands why these diseases, which cause people to progressively lose their motor functions, happen. We have discovered a new player in myelin diseases that was never considered before. “

Provided by University of Alberta