

Double duty: Immune system regulator found to protect brain from effects of stroke

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A small molecule known to regulate white blood cells has a surprising second role in protecting brain cells from the deleterious effects of stroke, Johns Hopkins researchers report. The molecule, microRNA-223, affects how cells respond to the temporary loss of blood supply brought on by stroke—and thus the cells' likelihood of suffering permanent damage.

"We set out to find a small molecule with very specific effects in the brain, one that could be the target of a future [stroke treatment](#)," says Valina Dawson, Ph.D., a professor in the Johns Hopkins University School of Medicine's Institute for [Cell Engineering](#). "What we found is this molecule involved in immune response, which also acts in complex ways on the brain. This opens up a suite of interesting questions about what microRNA-223 is doing and how, but it also presents a challenge to any therapeutic application." A report on the discovery is published in the Nov. 13 issue of the [Proceedings of the National Academy of Sciences](#).

RNA is best known as a go-between that shuttles genetic information from DNA and then helps produce proteins based on that information. But, Dawson explains, a decade ago researchers unearthed a completely different class of RNA: small, nimble fragments that regulate [protein production](#). In the case of microRNA, one member of this class, that control comes from the ability to bind to RNA [messenger molecules](#) carrying genetic information, and thus prevent them from delivering their messages. "Compared with most ways of shutting genes off, this

one is very quick," Dawson notes.

Reasoning that this quick action, along with other properties, could make microRNAs a good target for therapy development, Dawson and her team searched for microRNAs that regulate [brain cells'](#) response to [oxygen deprivation](#).

To do that, they looked for proteins that increased in number in cells subjected to stress, and then examined how production of these proteins was regulated. For many of them, microRNA-223 played a role, Dawson says.

In most cases, the proteins regulated by microRNA-223 turned out to be involved in detecting and responding to glutamate, a common chemical signal brain cells use to communicate with each other. A stroke or other injury can lead to a dangerous excess of glutamate in the brain, as can a range of diseases, including autism and Alzheimer's.

Because microRNA-223 is involved in regulating so many different proteins, and because it affects glutamate receptors, which themselves are involved in many different processes, the molecule's reach turned out to be much broader than expected, says Maged M. Harraz, Ph.D., a research associate at Hopkins who led the study. "Before this experiment, we didn't appreciate that a single microRNA could regulate so many proteins," he explains.

This finding suggests that microRNA-223 is unlikely to become a therapeutic target in the near future unless researchers figure out how to avoid unwanted side effects, Dawson says.

More information: www.pnas.org/content/early/2011/12/17/1217394109.abstract

Provided by Johns Hopkins University School of Medicine

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