New stroke treatment could prevent and reduce brain damage

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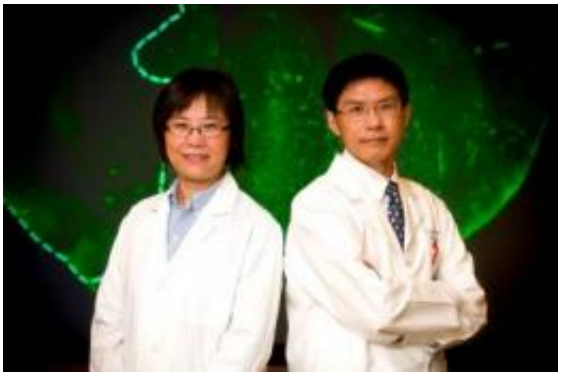

Zezong Gu, M.D., Ph.D., right, and Jiankun Cui, M.D., both assistant professors of pathology and anatomical sciences, are studying a new compound designed to stop the spread of brain bleeds and protect brain cells from further damage in the crucial hours after a stroke. Stroke is a leading cause of death in the US with more than 800,000 deaths occurring each year from stroke and other cardiac events. Credit: University of Missouri School of Medicine

Researchers at the University of Missouri have demonstrated the effectiveness of a potential new therapy for stroke patients in an article published in the journal *Molecular Neurodegeneration*. Created to target a specific enzyme known to affect important brain functions, the new compound being studied at MU is designed to stop the spread of brain bleeds and protect brain cells from further damage in the crucial hours after a stroke.

Stroke is a leading cause of death in the U.S. with more than 800,000 deaths occurring each year from stroke and other cardiac events. Other than surgery, existing emergency treatments for stroke victims such as the use of a tissue plasminogen activator (tPA) must be administered within hours of the stroke onset because of the risk for brain hemorrhaging. The injectable medication can only be used to treat the most common type of stroke that occurs when blood clots block blood flow to the brain, called ischemic stroke.

"For a stroke victim, time is a matter of life and death. While we are still in the research phase for this type of compound, we believe it could be combined with tPA in the future to buy ischemic stroke patients a longer window of time to receive emergency treatment," said Zezong Gu, MD, PhD, the article's corresponding author and assistant professor of pathology and anatomical sciences at the MU School of Medicine. The new compound being studied also has potential for use in patients experiencing hemorrhagic stroke, which is a less common type of stroke caused by bleeding within the brain, Gu said.

MU researchers collaborated with a team at the University of Notre Dame to study the effects of the new compound, a thiirane class of gelatinase selective inhibitors, on the function of a type of matrix metalloproteinase (MMP) enzyme, particularly MMP-9. MMP-9 is part of a group of more than 20 enzymes or MMPs that are known to contribute to many key pathological events in the brain after stroke, traumatic brain injury and other neurodegenerative events.

In 2005, Gu served as a lead author on a research paper published in the *Journal of Neuroscience* that identified MMP-9 as a promising target for development of therapeutic drugs for stroke patients. Since then, his lab at MU medical school's Center for Translational Neuroscience has been studying the function of MMP enzymes and how to inhibit the harmful effects of MMP-9.

"MMPs play a role in the structure of blood vessels in the brain and are also needed in the interactions between cells during development and tissue remodeling," Gu said. "Unregulated, the activity of these enzymes contributes to neurological disorders and stroke. With this compound, we've now confirmed a potential method to rescue the blood vessels from the damaging effects of MMP-9 and protect neurons at the same time."

MU researchers successfully used a model of ischemic stroke in mice and studied the effects of the MMP-9 inhibitor compound on brain activity after a stroke.

"Our lab at the Center for Translational Neuroscience is one of only a few in the United States that has successfully induced a blood clot in the brains of mice," said Jiankun Cui, MD, the article's lead author and assistant professor of pathology and anatomical sciences at the MU School of Medicine. "To be able to study the effectiveness of this potential new treatment under these conditions provides us with a highly unique set of data showing this compound can disrupt key harmful pathological events that occur after a stroke."

Provided by University of Missouri School of Medicine