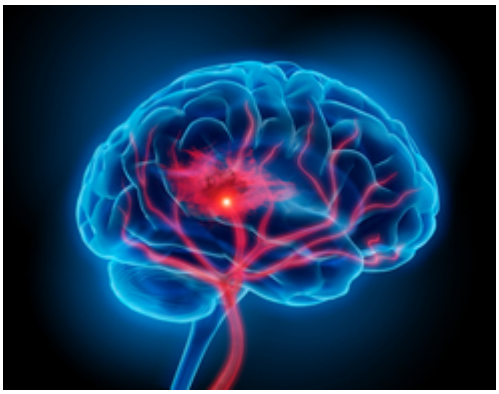
INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

PKC Inhibition to Allow Extended tPA Treatment for Stroke

TECHNOLOGY NUMBER: 7702



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Therapeutics and Vaccines
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OVERVIEW

Tissue plasminogen activator (tPA) remains the mainstay of treatment for patients with stroke

- Delivery of tPA beyond a 3-to-4-hour therapeutic window can cause bleeds and worsen outcomes
- Protein kinase C (PKC) inhibition can extend the time frame for tPA effectiveness

BACKGROUND

Stroke, or cerebrovascular accident (CVA), remains a leading cause of morbidity and mortality with limited therapeutic options. The current standard of care for patients with moderate to severe ischemic stroke is thrombolytic therapy with tissue plasminogen activator (tPA). This intervention can significantly improve neurological outcome if given within 3 to 4 hours of stroke onset, however tPA delivery after this therapeutic window causes vascular changes that cause bleeding and worsen patient outcomes. The mechanism for this hemorrhage is thought to be related to the cleavage of an inactive form of platelet derived growth factor C (PDGF-C) to an active form which increases brain vascular permeability. In patients who do not present to a medical facility within a short time after the onset of symptoms, clinicians are therefore unfortunately relegated mostly to providing supportive care. A need exists to better understand and prevent tPA induced hemorrhage with the goal of improving and extending the time frame over which thrombolytic therapy may be useful for stroke patients.

INNOVATION

Researchers at the University of Michigan propose that delivery of protein kinase C (PKC) inhibitors prior to or concurrent with tPA can significantly extend the window during which tPA

can be given to a stroke patient, thereby facilitating a faster and more complete recovery for those who do not present to a healthcare facility in the first 3 to 4 hours after the onset of symptoms. PKC inhibitors block PDGF-C cell receptors and can restore the integrity of the blood brain barrier (BBB), lower the risk of hemorrhagic transformation, and reduce infarct size. Protein kinase C inhibitors have already been known to control vascular permeability in blinding eye diseases such as diabetic retinopathy, and their effectiveness in preventing intracerebral hemorrhage has been reported in mouse models of thrombolytic stroke. The goal moving forward will be to use this approach to broaden the population of stroke patients who benefit from the favorable effects of tPA treatment.