Brilliant blue G may shine in treating traumatic brain injuries

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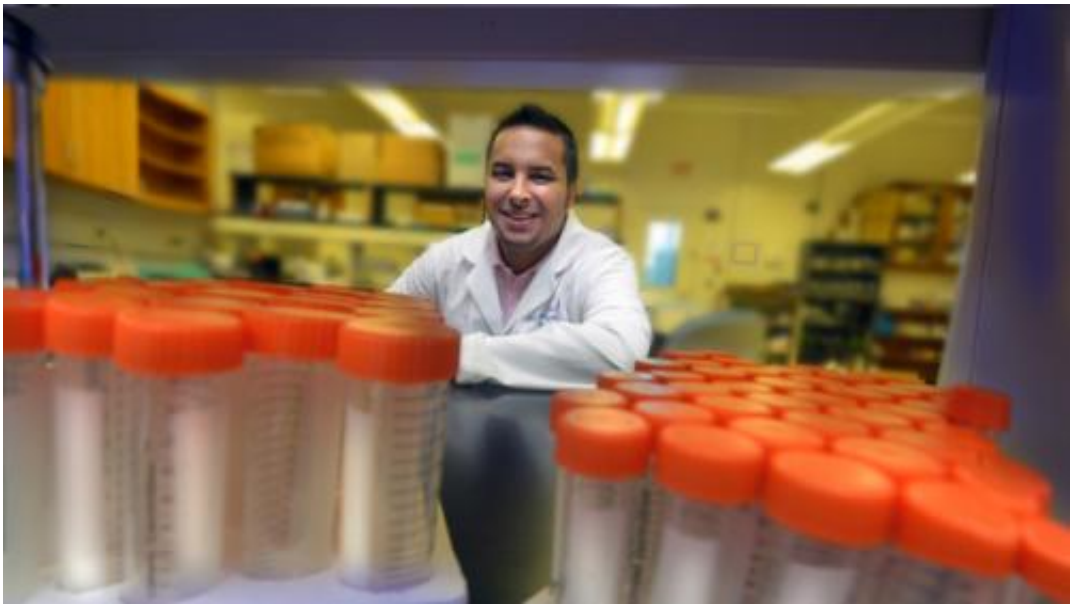

Vender and Neuroscientist Krishnan Dhandapani are Co-Principal Investigators on a new National Institutes of Health. Credit: Phil Jones

A close cousin of the dye that makes fabric, M&M's and sports drinks blue may improve recovery from traumatic brain injuries.

Falls, motor vehicle accidents, collisions, assaults, and war injuries result in more than 1.7 million Americans experiencing a traumatic brain injury annually, according to the Centers for Disease Control and Prevention.

While two -thirds of these injuries are relatively minor, nearly 40 percent of patients with severe brain trauma die as a result of damage that occurs after the original injury, as the brain attempts to heal within the closed confines of the skull, said Dr. John Vender, Vice Chairman of the Department of Neurosurgery at the Medical College of Georgia at Georgia Regents University.

Vender and Neuroscientist Krishnan Dhandapani are Co-Principal Investigators on a new National Institutes of Health-funded study to see if the dye brilliant blue G can intervene by temporarily blocking at least one immune response that leads to damaging and potentially deadly swelling in the hours and days after injury.

A focus is interleukin 1, a common pro-inflammatory cytokine that aids wound healing and repair. "Any time you cut your finger, you are going to have interleukin there," Dhandapani said. However in the brain, the MCG researchers are finding interleukin1 also promotes water retention, which drives swelling.

The intent appears positive: swelling opens up the pores of the brain's blood vessels, literally providing more room for infection fighters, blood clotting and other agents to move in, Vender said. "It's bringing in the supplies needed to fight the injury," added Dhandapani. However, the system designed to ramp up exponentially, can quickly overwhelm, affecting too much tissue and causing too much swelling.

"It's all a balancing act," said Dhandapani, and, in this case, stability is lost. "If interleukin is doing more harm than good at that early stage, let's temporarily block it," Dhandapani said.

That's where brilliant blue G appears to shine. They are retracing the steps following a traumatic brain injury to double check their findings that trauma activates NLRP3, a protein that drives the immune response,

which activates interleukin , which causes an immune response that significantly contributes to swelling. They'll also be looking again at the efficacy of brilliant blue G at stopping the crescendo by giving it up to eight hours after the initial injury in their rodent model.

If they are correct, measuring levels of interleukin 1 in the blood could identify intensive care patients at risk for brain swelling and the dye, whose nearly identical chemical cousin is consumed daily by millions, could be given to stop it. Ideally, brilliant blue G also could be given prophylactically to high-risk groups such as soldiers and football players, Vender and Dhandapani muse.

"It's clinically safe, people are using it, so we know that we can use it. It's not going to cause toxicity and it's relatively inexpensive and easy to store," Dhandapani said. In fact, the only side effect the researchers have seen is, at therapeutic doses, mice in the study temporarily take on a blue hue.

It's also one of the first therapies to approach the problem early and at the molecular level. While improvements in prevention, such as better helmets, as well as lessons learned primarily from armed conflicts – such as field resuscitation, rapid transport, and the concept of the golden hour – have advanced survival rates for patients, "What we have not been able to do is prevent that 40 percent loss of function that is still occurring," said Vender.

As a neurosurgeon at a Level One Trauma Center, Vender performs hemicraniectomies where he temporarily removes a portion of the skull to hopefully avoid the additional damage that occurs when the swelling brain presses up against the hard, and usually protective, skull, following a traumatic brain injury. While the procedure has proven helpful, by the time increased intracranial pressure merits such a maneuver, more brain tissue already has sustained damage.

Vender and Dhandaphani want to intervene sooner. "What Kris is doing in the lab is blocking the process before it gets to the point where it hurts the brain tissue," Vender said. "That is what is exciting about it."

Their search for better therapies began by looking for differences in the cerebral spinal fluid of patients with and without a traumatic brain injury and finding higher levels of interleukin-1 was a major one. "We want to figure out if the interleukin we found in the cerebral spinal fluid is causing problems or are other problems causing interleukin to go up," Dhandapani said. They are betting it's the former.

Provided by Medical College of Georgia