To the brain, straight from the vein: IV treatment for TBI

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Steven Stice, left, and Lohitash Karumbaiah Credit: UGA

A team of researchers from the University of Georgia's Regenerative Bioscience Center has found that neural exosomes—"cargo" molecules within the nervous system that carry messages to the brain—can minimize or even avert progression of traumatic brain injury when used as part of a new cell-to-cell messaging technology.

The finding could result in the first delivery platform and regenerative treatment for TBI.

The research was reported on Nov. 27 in the *Journal of Neurotrauma* and outlines significant steps in providing data for industry development and commercial manufacturing of a regenerative TBI-IV therapy.

The new restorative technology contains bio-manufactured exosomes that can be stored on the shelf and given as an injection into a vein. Once injected, the exosomes become message mediators to reset, regenerate and coordinate communication with both neighboring and distant cells. As a result, this novel treatment showed improved functional recovery in rats after TBI.

"The technology takes full benefit of the desirable properties of a neural stem cell therapy without introducing cells into patients," said Steven Stice, Georgia Research Alliance Eminent Scholar and D.W. Brooks Distinguished Professor in the College of Agricultural and Environmental Sciences. "We are working toward a therapeutic that has a multifunctional promise to repair brain injury and be producible in a cost-effective, off-the-shelf drug format."

Traumatic brain injuries can be difficult to detect because each TBI patient presents a unique set of circumstances determined by injury timeline and severity, as well as individual characteristics such as age, gender and occupation. With this potential new technique, RBC researchers hope to boost the brain's natural ability to recover and provide physicians with a treatment that can be administered immediately in cases of severe TBI.

"Mechanistically, TBI is a physician's nightmare," said Lohitash Karumbaiah, associate professor of regenerative medicine in UGA's College of Agricultural and Environmental Sciences and one of the publication's lead authors. "Because there are so many things going on in the brain, you can't really exactly pinpoint what is going wrong, and without therapies to immediately improve recovery, the situation becomes extremely complex."

For those affected by TBI, treatment could be administered at the time of injury with IV fluids. Using multiple low-dose, intravenous injections, the novel treatment is designed to speed up regeneration of neurons and supporting cells following injury.

"Administrating exosomes into a patient's IV drip would always be preferable to invasive brain surgery," Karumbaiah said. "What we can do is give physicians a fighting chance to regulate the inflammatory response of TBI, rather than trying to treat it after it occurs."

Another application the team has considered is the use of exosome technology as a preventive management program for all levels of TBI, including mild and moderate concussions that could minimize or prevent future damage.

Licensed to and under development by Aruna Bio, one of UGA's first Innovation Gateway startups, the exosome technology has already captured the interest and financial support of the Georgia Research Alliance's Venture Fund, one of the largest venture capital funds in the state. The GRA Venture Fund, along with other investors, contributed to the $13 million in common stock financing recently announced by Aruna Bio.

"Drug development for acute TBI has suffered so many clinical failures and will need to take an imminent paradigm shift toward a more targeted and personalized treatment," said Stice. "We still have a lot to learn, but our success could create the tipping point."

More information: Min Kyoung Sun et al, Extracellular vesicles mediate neuroprotection and functional recovery after traumatic brain injury, *Journal of Neurotrauma* (2019). DOI: 10.1089/neu.2019.6443

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