Research into brain's ability to heal itself offers hope for novel treatment of brain injury

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Innovative angles of attack in research that focus on how the human brain protects and repairs itself will help develop treatments for one of the most common, costly, deadly and scientifically frustrating medical conditions worldwide: traumatic brain injury.

In an extensive opinion piece recently published online on *Expert Opinion on Investigational Drugs*, Henry Ford Hospital researcher Ye Xiong, M.D., Ph.D., makes the case for pioneering work underway in Detroit and elsewhere seeking to understand and repair brain function at the molecular level.

"To date, all attempts at treating traumatic brain injury with experimental drugs have failed once testing moved from animal studies to clinical trials in humans," Dr. Xiong explains. "Although this is disappointing, we believe innovations now at the preclinical stage hold great promise for a deeper understanding of traumatic brain injury and how to treat it."

Also known as TBI, traumatic brain injury most commonly results from a sudden, violent blow to the head, in some cases driving broken bone into the brain, or from a bullet or other object piercing the skull and entering the brain.

This trauma sets off a complex "cascade" of reactions in the brain that

can impair thinking and reasoning, behavior and movement.Each year, at least 10 million TBIs that are serious enough to result in hospitalization or death occur around the world.

Most attempts at treatment have targeted the physical damage with drugs aimed at protecting neurons - the cells that carry messages from the brain to the rest of the body - from further damage. But while such attempts have shown promise in animal studies, they've all failed to help human patients.

Over the past three decades, more than 30 such clinical trials have ended in failure.

More recently, evidence has been amassed by researchers showing that the human brain has "a significant, albeit limited" ability to repair itself both physically and functionally, including:

- Angiogenesis - the creation of new blood vessels.
- Neurogenesis - the formation of new nerve cells.
- Oligodendrogenesis - the development of several types of cells including those that make up the myelin sheath, a protective coating on parts of nerves.
- Axonal sprouting - the process of in which undamaged axons, threadlike parts of nerve cells that carry signals to other cells, grow new nerve endings to relink damaged neurons.

The new approach to TBI therapy described by Dr. Xiong aims at enhancing these restorative, or "neuroplastic," processes as they work together to improve neurological recovery.

"Significant advances in the understanding of the mechanisms underlying TBI's behavioral, cognitive or psychiatric effects have been made, and the use of cell-based and pharmacological interventions to

improve symptoms, function and outcome is still under development," Dr. Xiong explains.

Among interventional drugs now in early clinical trials are:

- Glibenclamide. Already best known for treatment of type 2 diabetes, it has recently been found to significantly reduce brain swelling and bleeding after ischemic stroke, suggesting potential use for treating TBI.
- Minocycline. Derived from the antibiotic tetracycline, it has been shown in different dosages to provide both short-term and long-term benefits in treating closed head injuries in mice.
- Statins. Widely used to reduce cholesterol levels, studies at Henry Ford Hospital have demonstrated that these drugs restore cognitive function after TBI in rats.

Other promising investigational biologics and drugs that are now in promising preclinical development at Henry Ford include thymosin beta 4, exosomes recombinant human tissue plasminogen activator and microRNAs.

"Although it is still important to further investigate neuroprotective treatments for TBI, these novel, neurorestorative or neuroplastic approaches will facilitate development of treatments for TBI with the ultimate goal of reducing brain injury, promoting brain repair and remodeling, and eventually improving functional recovery and quality of life," Dr. Xiong concludes.

More information: Investigational agents for treatment of traumatic brain injury, Posted online on March 1, 2015. (doi:10.1517/13543784.2015.1021919) informahealthcare.com/doi/abs/… 3543784.2015.1021919

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