Neuroprotecting and Repairing Injured Retina and Optic Nerve with ECM

McGowan Institute for Regenerative Medicine affiliated faculty member Michael Steketee, PhD, assistant professor of ophthalmology, UPMC Eye Center and the Fox Center for Vision Restoration, and McGowan Institute deputy director Stephen Badylak, DVM, PhD, MD, professor in the Department of Surgery and director of the Center for Pre-Clinical Tissue Engineering within the McGowan Institute, are the co-principal investigators of a 3-year, $1 million Department of Defense Congressionally Directed Medical Research Programs, Vision Research Program Translational Research Award. McGowan Institute director William Wagner, PhD, Professor of Surgery, Bioengineering, and Chemical Engineering at the University of Pittsburgh, and Kia Washington, MD, assistant professor in Pitt’s Department of Plastic Surgery, are the co-investigators of this project entitled, “Applying extracellular matrix technology to neuroprotect and to repair injured retina and optic nerve.”

In modern warfare, blast injuries are the most common wounded-in-action injuries accounting for approximately 60% of all injuries as of July 2009 with up to 40% of blast injuries expressing concomitant eye injuries. Ocular blast trauma accounts for 80% of all ocular war injuries.

After trauma to the eye or optic nerve, which connects the eye to the brain, patients must be evacuated first to a combat support hospital and then to the United States for specialized microsurgery usually not possible in field hospitals. This time from injury to treatment in the United States can be from 2-3 days to 4 weeks depending on the severity of the patient’s other injuries. During this time, inflammation in the eye can greatly increase the scope of the injury, often more so than the original injury. This secondary inflammation often results in scar formation, increases the likelihood and the scope of permanent vision disability.

Scarring due to secondary inflammation is a persistent clinical problem since medical experts lack a therapeutic that can reduce harmful inflammation in the eye. The only current treatment is injecting steroids, which limits all inflammation often causing other undesirable outcomes. Inflammation comes in different flavors: inflammatory or tissue destructive and anti-inflammatory or tissue constructive. By eliminating all inflammation, we also eliminate the good tissue constructive inflammation.

To solve this problem, this project proposes to use extracellular matrix (ECM) technology in an injectable hydrogel format that can be injected into or around the eye and in a convenient wrap format for treating the injured optic nerve. These technologies are designed to stabilize retina or optic nerve injury, reduce scarring, and increase the potential for vision preservation.
How does ECM work? ECM is the support structure surrounding the cells of tissues and organs containing signals that interact with cells and aid in defining the organ. By removing the cells from the tissue or organ, it is possible to create an interactive material, that when placed back into an injury, interacts with the cells and directs positive tissue reconstruction. This is partially due to altering the normal immune response from inflammatory to anti-inflammatory and by recruiting the body’s natural stem cells. ECM materials have been used to treat over 4 million patients and are currently being used by the University of Pittsburgh in collaboration with the Department of Defense for treating traumatic skin, bone, and muscle injuries. By applying two forms of ECM materials, a hydrogel capable of direct injection into the eye and a biohybrid wrap to place around the optic nerve, the team is confident they can stabilize a wide variety of ocular injuries in combat field hospitals.

ECM technologies are capable of being applied to a large range of other injuries besides ocular trauma, including peripheral nerve and traumatic brain injury. The potential health benefits range from vision preservation to ocular reconstruction and vision restoration. While adverse events happen following injury, McGowan Institute researchers are confident that these technologies have minimal risk. ECM scaffolds, when prepared appropriately do not cause an immune response, and are quickly integrated into the body. There is also potential for these technologies to be translated to age-related diseases such as macular degeneration. The research team assembled has the experience and the expertise to develop these technologies, translate the solutions to humans, and to make a difference in vision preservation and restoration after traumatic eye injuries. The research team is confident that these technologies will begin the translation process into humans by 2019.