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Sight-Restoring Therapy for Corneal Injuries Sustained on the Battlefield From Chemical Warfare

Principal Investigator: DI GIROLAMO, NICK
Institution Receiving Award: NEW SOUTH WALES, UNIVERSITY OF
Program: VRP
Proposal Number: VR200025
Award Number: W81XWH-21-1-0883
Funding Mechanism: Investigator-Initiated Research Award - Funding Level 2
Partnering Awards:
Award Amount: $725,733.00

View Technical Abstract

PUBLIC ABSTRACT

Good eye health is essential for exquisite vision. Service personnel rely on exceptional vision to conduct military-specific duties both on and off the battlefield. On the battlefield, eyes are generally protected with appropriate eyewear; even so, ocular injuries are still common and account for up to 13% of all battlefield trauma. The cornea is the eye's outer shell, it's the part of the eye that is very painful to touch as it contains many sensory nerve fibers. The cornea is also the clear window to the eye and its transparency is preserved by a special population of cells called stem cells. These stem cells and their descendants (corneal epithelial cells), along with the nerves that populate this tissue, interact with one another throughout life. Battlefield, terror, industrial, and domestic injuries in the form of a mechanical, thermal, or chemical insult can inflict significant damage to the cornea, often targeting the stem cells and nerves that support this important sensory organ. When the trauma is minor, standard medication is available and is applied to resolve the wound in a timely manner. However, when the trauma is severe, to the extent that the stem cells and their supporting nerves are depleted or destroyed, this can have catastrophic consequences for the victim, including the development of chronic, painful corneal defects that do not heal and cannot be treated with standard medical interventions; not even a corneal transplant can be offered to save or restore sight. In such cases a disease called Limbal Stem Cell Deficiency (LSCD) can ensue in which the patient can only be treated with a specialized stem cell therapy.

In the past, we have helped such patients through the application of a novel stem cell transplantation strategy conducted via a clinical trial. Several of these trials have and are being conducted around the world, however, the success rate varies from 0%-70%. This is because the cause of LSCD varies, there is no standard treatment where one treatment can be applied to all patients, the cells being transplanted are carried to the patient's eye(s) on foreign biologicals or synthetic (man-made) materials, the disease is difficult to diagnose, we do not know what happens to the implanted stem cells, we do not have a good clinical measure and/or monitor of how successful the treatment is/has been, and current stem cell treatments are expensive and not commercially available in the US, or are still in the experimental phase of development. This means there are significant knowledge and technical gaps to fill. In the short term, these unknowns will be addressed in the current proposal with the aid of animal models of chemical-induced LSCD that simulates the disease that develops in humans, as well as the application of a technically advanced computer program we developed that will measure nerve characteristics in a mouse cornea within seconds. We hope to adapt this system for use on human corneas to help clinicians monitor disease progression and therapeutic outcome. With this information in hand we will be better positioned to conduct the next phase of our research program, which involves the delivery of a much improved longer-lasting therapy for current and retired military personal and the American and global public with current unmet medical needs. Notably, our proposal is ambitious, creative and innovative, and the experiments outlined are challenging; nonetheless we have formed a world-class gender- and career-balanced coalition of investigators (two clinician MDs and three basic scientist PhDs) with overlapping and complementary expertise to execute the stated aims, which include: (1) Identify, locate, and measure corneal nerve features in mice with chemical-induced LSCD; (2) Determine if corneal nerve fibers align with epithelial cells in healthy and diseased mouse corneas; (3) Determine the outcome of a new stem cell transplant strategy in mice with chemical-induced LSCD.

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The CDMRP originated in 1992 via a Congressional appropriation to foster novel approaches to biomedical research in response to the expressed needs of its stakeholders-the American public, the military, and Congress.

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