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Macrophage Migration Inhibitor (MIF) Therapeutics for Neuroprotection and Prevention of Scar in Traumatic Retinal Detachment

Principal Investigator: CEBULLA, COLLEEN
Institution Receiving Award: OHIO STATE UNIVERSITY, THE
Program: VRP
Proposal Number: VR170167
Award Number: W81XWH-18-1-0805
Funding Mechanism: Technology/Therapeutic Development Award
Partnering Awards:
Award Amount: $1,905,666.00

View Technical Abstract

PUBLIC ABSTRACT

Retinal detachment (RD) is a prevalent cause of blindness that is common after ocular injury to military personnel. RD is the separation of the neural tissue that senses light (retina) from the underlying layers of the eye that supply it with blood and nutrients, making it non-functional. It is caused by a tear or trauma to the retina. Permanent vision loss occurs due to (1) death of retinal cells known as photoreceptors and (2) formation of excessive scar tissue in and around the retina, known as proliferative vitreoretinopathy (PVR). PVR is the most common cause of failure of RD surgery, and there are no effective pharmaceuticals to prevent it, although several drugs have been tried. Steroids are used clinically and have some weak benefit.

The proposed research will investigate the effects of drugs that target an inflammatory protein, macrophage migration inhibitory factor (MIF), which is produced at high levels in PVR and is increased by steroid use. Our recently published data show that the MIF inhibitor ISO-1 prevents death of photoreceptors and reduces gliosis in the retina of a mouse RD model. In addition, blast injury, which is common in military trauma, damages neurons by activating NMDA receptors and causing excitotoxic damage. We have also shown that MIF is increased in chick retina that is damaged by NMDA and that ISO-1 protects against that damage.

The proposed research will test the ability of different clinically relevant MIF inhibitors to block photoreceptor death and abnormal healing after RD or NMDA damage in different animal models. One of these drugs, ibudilast, has already been approved for human use in Japan as an anti-inflammatory agent and is currently undergoing clinical trials in the United States as a neuroprotective agent for several neurologic diseases. Another drug, CPSI-1306, is a derivative of ISO-1 and displays improved clinical properties and a safer profile over its predecessor. Since the eye is an extension of the brain, we predict these drugs will be promising for retinal trauma. This research will have considerable promise for treating ocular disease triggered by military injuries. We hope it will provide ground work for a clinical trial in patients, which could one day lead to therapeutics that could prevent vision loss in military and civilian patients with several retinal diseases.

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