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NorLeu3Angiotensin (1-7) Promotes Nonfibrotic Healing in Ocular Globe Injury Models

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Institution Receiving Award: UNIVERSITY OF SOUTHERN CALIFORNIA
Program: VRP
Proposal Number: VR200176
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View Technical Abstract

PUBLIC ABSTRACT

Injury(ies) to the eye can vary from mild to severe conditions. Eye injury(ies) involving the cornea, the clear layer covering the eye, may affect the ability to return to the pre-injured state. The ability to heal back to the pre-injured state is determined by the extent of the injury, which includes the depth and size of the wound. When the injury has penetrated through the cornea, which is often referred to as "Full Thickness" injury, these types of injuries often have scarring. Scar formation or fibrosis can distort vision and, therefore, the reduction of fibrosis is more likely to restore visual function.

Patients afflicted by eye injuries often experience significant discomfort, irritation, swelling, and/or pain. The breakdown of the corneal barrier can also increase the risk for infections, which can cause permanent vision loss. Current treatments for corneal injury include reduction of pain and swelling with the application of topical antibiotics. Other medical treatment can include application of an eye patch. Unfortunately, none of these medical measures can accelerate corneal wound healing.

The American Academy of Ophthalmology (AAO) estimates that there are 2.5 million eye injuries occurring in the United States, yearly. It is reported that many of these injuries lead to permanent vision loss. Management of these injuries requires rapid treatment, which is dependent upon the size and depth of the wound. Immediate wound closure to the pre-injury state has the best chance to regain visual function. Currently, there is no Food and Drug Administration (FDA)-approved drug that is capable of accelerating cornea wound healing. NorLeu^3Angiotensin (1-7) eye drop is able to accelerate corneal healing without fibrosis, which can minimize the potential for ocular scarring and visual distortion. This property can maximize the potential to restore visual function.

This proposal aims to demonstrate that treatment with NorLeu^3Angiotensin (1-7) eye drop is both safe and effective in accelerating corneal healing for injuries that has penetrated the entire length of the cornea. We believe NorLeu^3Angiotensin (1-7) eye drop treatment can promote healing while minimizing corneal haze and fibrosis, which can distort vision.

This proposal will use NorLeu^3Angiotensin (1-7) eye drop in preclinical models of ocular globe injury. We propose to identify the conditions that will lead to maximal ocular wound healing in the absence of corneal haze or scarring. This proposal will also evaluate whether more frequent dosing will further improve the ability to accelerate corneal healing. We currently have data showing that NorLeu^3Angiotensin (1-7) eye drops can accelerate corneal wound closure within 4 days, where the cornea returns back to near-normal architecture within 28 days. Furthermore, the NorLeu^3Angiotensin (1-7)-treated wounds were found to be twice as strong as groups receiving placebo. It is not known how effective NorLeu^3Angiotensin (1-7) eye drop is in more severe injuries, such as open globe injuries. To address this issue, this proposal will evaluate the concentration of NorLeu^3Angiotensin (1-7) eye drop that is required to rapidly close these types of injuries when used alone or in combination with bandage contact lens (BCL). We will also determine the number of treatments per day that will maximally accelerate wound healing. Finally, we will evaluate whether NorLeu^3Angiotensin (1-7) eye drop can be combined with BCL. As we gather this information, we will determine how NorLeu^3Angiotensin (1-7) eye drop is able to exert its biological properties. To do this, we will evaluate the molecule changes in the treated eyes and compare them with placebo controls.

The ability to prevent permanent visual lose can significantly reduce healthcare costs. At the end of the proposed 36-month project, we will have information for the best way to use NorLeu^3Angiotensin (1-7) to treat wounded warriors who sustain eye injuries. In combination

with our other development with NorLeu^3Angiotensin (1-7), our team will be in position to start phase 2 clinical trials at the completion of this proposal.

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