Nanofiber-Reinforced Hydrogels for Ocular Repair

Technology Description

The increasing frequency of ocular injuries sustained on the battlefield coupled with the storage and application issues associated with the current standard of care, human amniotic membrane (HAM), has prompted Luna to develop "BIOcular™", a synthetic bandage for the treatment of the ocular surface following traumatic injury. In this biomaterial, the healing properties of amniotic membrane are mimicked in an *electrosprayed* hydrogel material, and the mechanical properties are enhanced with nanofiber reinforcements that are *electrospun* to mimic extracellular matrix. This material is optically clear, compatible with human corneal epithelial cells, and has controllable resorption properties depending on the desired application. Luna's BIOcular™ dressings are also designed to be compatible with photochemical tissue bonding (PTB) techniques to avoid the necessity of sutures for application, and have the potential to deliver therapeutics to the injured site in a controlled fashion.

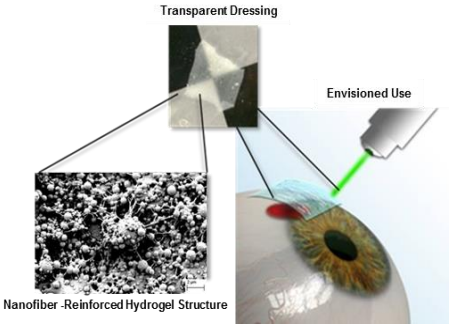

Figure 1. Luna's BIOcular™ is designed for sutureless application to promote regeneration of the ocular surface**.**

Properties of Luna's Ocular Biomaterial

- Mimics natural ocular structure
- Is transparent, biocompatible, and biodegradable
- Conducive to epithelial and endothelial cell growth
- Cost-effective and easy to store
- Can be sutured into place or adhered via PTB
- Can be used to deliver therapeutics or growth factors with sustained release
- Can be produced at multiple sizes and thicknesses

Luna has characterized the optical, biological, and mechanical properties of BIOcular™ dressings to ensure they meet the needs of practicing ocular surgeons for corneal wound healing or open globe stabilization applications. UV-Vis Spectroscopy was used to quantify transparency through the hydrated constructs at 550 nm and indicated that up to 85% transparency was achieved in the final prototype dressings. Additionally, the refractive index of the dressing is 1.335, nearly identical to that of the native corneal tissue (1.37). Biocompatibility with human corneal epithelial cells and bovine corneal endothelial cells was confirmed using a lactate dehydrogenase assay, and alignment of the nanofiber component was quantified as an anisotropy value calculated using the FibrilTool Plugin for ImageJ analysis. Prototype dressings were provided to Dr. Andrew Eiseman, former Chief of Oculoplastic and Orbit Service at Walter Reed Army Medical Center and current practicing oculoplastic surgeon at the Medical University of South Carolina, for his professional opinion on handling properties, transparency, and overall quality. Dr. Eiseman praised their ease of hydration and handling, flattening on a surface, as well as the uniform structural integrity of the dressings. Most BIOcular™ dressing formulations are robust enough to withstand suturing, but this product also been designed to be compatible with sutureless adhesion techniques

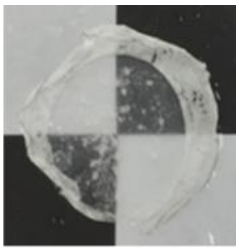

Figure 2. Luna's BIOcular dressings demonstrate favorable transparency when hydrated

Indications for Use

The BIOcular™ dressing is being developed as a platform technology for a family of products to be adapted to suit a multitude of ocular wound healing applications. Luna is developing nanofiber-reinforced hydrogel BIOcular dressings of various chemistries to achieve a variety of mechanical, optical, and biological properties. These dressings can be used for the treatment of corneal-surface wounds, stabilization of severe open-globe injuries, or sustained delivery of relevant therapeutics to the ocular surface. These dressing can also be layered to fill thicker ocular defects, loaded with antibiotics and antimicrobials to treat persistent corneal ulcers, or seeded with cells to stimulate corneal regeneration.

Technology Status

The BIOcular™ dressing is currently at a technology readiness level (TRL) of 4. Luna has completed a Phase I Army-funded SBIR program developing dressings for corneal surface regeneration and has started a Phase II program that focused on scaled production and *in vivo* validation of prototype functionality. Luna has also completed a second Phase I program utilizing alternate, more robust, polymeric dressings for the closure of severe open-globe injuries and was selected for Phase II funding to validate *in vivo* performance of these prototypes as well.

Additional Product Features

Customizable Properties: Luna has developed a library of bandages using various nanofiber chemistries to achieve an array of resultant properties. Luna has demonstrated control over water permeability, transparency (60%-90%), tensile strength (1-27 MPa), peak strain (0.08-0.6), and elastic moduli (1-200 MPa), all dependent on sample chemistry.

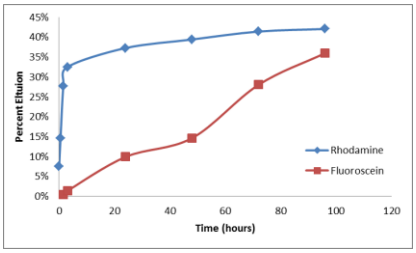

Figure 3. Elution of fluorescent drug-analogs from nanofiber dressings

Therapeutic Delivery: A majority of the work conducted to-date has focused on the fabrication and characterization of the nanofiber-reinforced hydrogel structure of these BIOcular™ dressings. However, Luna has also investigated the use of nanofiber based dressings for drug delivery, definitively demonstrating the loading and elution of fluorescent drug-analogs from electrospun nanofiber dressings with both burst and zero-order release kinetics (Figure 3). The ability to controllably deliver therapeutics to the ocular surface over time would improve drug residence time as compared to standard eye drops that are cleared quickly through the lacrimal system.

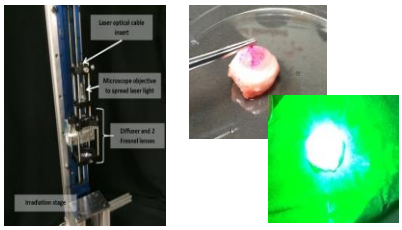

Figure 4. Luna has developed PTB protocols to suturelessly adhere dressings to the corneal surface

Sutureless Adhesion: Luna is also developing dressings that include rose bengal (a photoactive dye) for sutureless adhesion to the ocular surface using photochemical tissue bonding techniques. Rose Bengal is activated with the energy of 532 nm (green) light through Luna's custom designed light delivery system (Figure 4) to initiate bonding to the corneal surface.

Manufacturing Capability

Preliminary iterations of the dressings described above have been fabricated using standard benchtop electrospinning production methods. Recently, Luna has developed needle-free production techniques that provide the ability to form these unique matrices at a commercially relevant scale. Using a needle-free system like the Elmarco NanoSpider® NSLab system (Figure 5) allows the production of large sheets of nanofibers in a rapid and repeatable manner. The concentrations, voltages, and capture distances will remain identical through scale up from prototype to commercial scale production using various NanoSpider® equipment, significantly simplifying the process and reducing the cost of production. This is an important advancement for nanofiber-based dressings, as scale-up has been a limitation for these unique products for much of the last 20 years. Luna has developed multiple compatible methods for introducing the hydrogel component into these electrospun nanofiber mats.

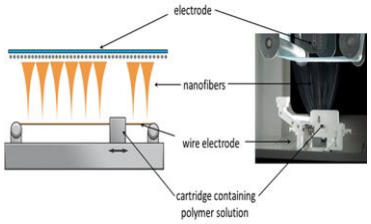

Figure 5. The Elmarco NanoSpider will simplify scale-up of BIOcular™ dressing production

This work was supported by US Army Contracts W81XWH-16-C-0010, W81XWH-14-C-0028, W81XWH-15-C-0139, and W81XWH-15-C-0010. The views, opinions, and findings are those of the author(s) and should not be construed as official Army position, policy or decision unless designated by other documentation.