Antimicrobial Silk Ocular Drug Delivery Implant for Chronic Posterior Segment Diseases

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PUBLIC ABSTRACT

In the United States, about 8% of the population has diabetes mellitus. For Veterans, the percentage with diabetes triples to nearly 25% (1.5 million persons). Diabetic retinopathy is a well-recognized complication that affects many persons that have diabetes for more than 10 years. After 15 years, about 10% of patients with diabetes develop severe vision loss, and about 2% become blind. Diabetic retinopathy is characterized by formation of new unhealthy, freely bleeding blood vessels leading to damage and scarring to the retina, the inner lining along the back of the eye that enables vision. Treatment of diabetic retinopathy can reduce vision loss by more than 90%. The emergence of medications that prevent abnormal blood vessels from forming in the eye, anti-vascular endothelial growth factor (anti-VEGF) drugs, have been very effective, but necessitate the need for monthly injections of the medication directly into the eye. Delivering anti-VEGF drugs by monthly injection keeps patients trapped in a cycle of constant maintenance and travel to specialized ophthalmologists with experience in diseases of the retina to receive these sight-saving medications; this method of delivering care is relatively expensive. Repeated intraocular (directly into the eye) injections also carry the risk of complications that can lead to loss of sight including infections within the eye, bleeding, damage to the retina leading to its detachment, and increased pressures within the eye. Development of a safe, infection-resistant, refillable, and long-term implantable intraocular device has the benefit of delivering constant therapeutic levels of drugs directly to the site of action without the side effects of systemic or intraocular injections. These types of devices would also decrease the need for frequent physician visits and monthly intraocular injections.

The devices will be generated using silk materials that have been studied by the Principal Investigator, Dr. Kaplan, along with Dr. Omenetto, and who have demonstrated silk's unprecedented versatility in biomedical engineering and high technology applications. Silk has the desirable properties of strength, lightweight, engineered flexibility and plasticity (able to undergo physical changes), and remarkable biocompatibility, including recent Food and Drug Administration approval for medical devices. Yet any device that crosses from the skin or eye (where bacteria normally live) into a sterile site will be at risk for infection. To greatly diminish the risk of infections, the silk-based device will be permanently coated with a non-leaching antimicrobial N,N-hexyl,methyl polyethylenimine (HMPEI). This HMPEI "spikey polymer" impales and kills viruses, bacteria, and fungi if they try to stick to and grow on the implant; it prevents devices from infection. Drs. Behlau and Klibanov have demonstrated the successful attachment of HMPEI to poly(methyl methacrylate) and titanium, materials used for implantable ocular and medical devices. In a recent collaborative effort, we have successfully bonded this antimicrobial coating, HMPEI, to surface modified silk that enabling HMPEI's attachment. Dr. Duker's ophthalmology expertise in the diagnosis, imaging, and management of vitreoretinal diseases provides rapid clinical translational guidance for our project plans. We have the combined expertise to develop a novel and safe sustained drug delivery system for the eye and adnexa for rapid clinical use, with broad applicability, and with significantly reduced susceptibility to infections.
The design of the silk-based implant is novel by incorporating three very different functions and will be manufactured as a one-piece device, entirely out of silk. On the outside of the eye, a small, self-sealing, refillable port will exist through which medication will be delivered. The injected anti-VEGF medication will then go through an impermeable delivery channel to a permeable drug reservoir that will be able to deliver 3 months of medication at the same rate and continuously. In addition, the anti-VEGF will be loaded in a silkwater-based gel that will enable the medicine to be made up in a tiny volume and keep it stable for months. We will then coat the entire implant with our antimicrobial coating, HMPEI, to safeguard it from infection. This new antimicrobial silk-based delivery system will not only decrease the burden of anti-VEGF treatments, but also maximize the medication's therapeutic benefit and safely.

The development of an antimicrobial HMPEI-silk ocular implant would provide optimal and safe delivery of long-term medication that will be comfortable, decrease the number of outpatient visits to just a few a year, and be relatively less costly. We may be able to use less medication if delivered continuously and optimally, while achieving greater therapeutic benefit. This technology may prove not only sight-saving, but cost-saving in the prevention of blindness from diabetic retinopathy and other disorders involving the retina with broad applicability to other diseases that occur in body sites that limit penetration of medication.