



STEIN EYE INSTITUTE  
DEPARTMENT OF OPHTHALMOLOGY  
DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA  
100 STEIN PLAZA  
LOS ANGELES, CALIFORNIA 90095-1722

April 15, 2023

The Independent Citizen's Oversight Committee (ICOC)  
California Institute for Regenerative Medicine (CIRM)  
1999 Harrison Street, Suite 1650  
Oakland, CA 94612

**Application: TRAN1-14649**  
Project Title: Extracellular Vesicle-Based Therapy for Corneal Scars  
PI Name: Sophie Deng, MD, PhD

Dear Members of the Board,

We thank the Grants Working Group for their critical review of our research proposal and positive comments. We would like to take this opportunity to emphasize important aspects of our proposal and ask for the ICOC's consideration to fund this project at the upcoming April 2023 Board Meeting.

### **Unmet Medical Need**

Corneal stromal scars caused by injuries or infection is the leading cause of corneal blindness globally. An estimated 4.9 million people are blind in both eyes, and an additional 23 million are blind in one eye due to corneal opacity. Corneal transplant is the only available sight-restoring treatment. Its effectiveness for scars caused by injury or infection is limited.

1. California's population is particularly susceptible to disadvantageous social determinants of health with race, ethnicity, financial stability, insurance, geographic region, and educational attainment identified as key predictors of adequate vision care. Corneal transplant is a highly specialized surgical operation requires a skilled corneal surgeon, ancillary staff, and specialized infrastructure. Additionally, patients must attend regular follow-up appointments after the surgery indefinitely. These requirements act as significant barriers to accessing care. **The treatment proposed in this application offers an alternative solution to corneal transplant to address vision loss caused by corneal scars, eliminating disparities in access to care by reducing or eliminating these barriers.**
2. **Half of the cornea grafts performed for corneal scars resulted from infection and injury do not survive beyond 10 years**, and the success rate of a second corneal transplant is only 22% and 11% at 5 and 10-year follow-up, respectively, contrary to a reviewer's comment that corneal transplant lasts for 10-20 years.

3. Corneal transplantation carries blinding complications, including expulsive suprachoroidal hemorrhage and endophthalmitis, while postoperatively, wound dehiscence, infection, and glaucoma could result in vision loss. The risk of glaucoma following corneal transplant is as high as 22%.

**An effective and accessible therapy that can prevent or reduce corneal scarring to preserve vision without the risks of blinding complications is an unmet medical need.** The proposed therapy using extracellular vesicles is designed to address this unmet medical need.

### **Project Design and Feasibility**

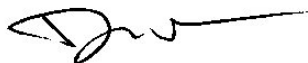
We are delighted to learn that all reviewers have found the proposed project and timeline to be feasible. The proposal aims to investigate the mechanism of action and biomarkers of extracellular vesicles. Additionally, we plan to determine the optimal route and dose of delivery and assess whether extracellular vesicles could treat established scars and alkaline burned corneas, thereby expanding the target product profile.

### **Potential to Change the Treatment Paradigm**

As pointed out by a reviewer, penetrating keratoplasty to treat corneal scars has been performed since early 1940s, with surgical approaches, postoperative management, and outcomes remaining largely unchanged for the past 40 years. In contrast, the outcomes of other solid organ transplants have greatly improved as a result of technological advances. Regenerative medicine, including cell and tissue regeneration, has become the focus of future therapeutic development for replacing transplantation for other organ systems. The proposed therapy aims to regenerate normal corneal tissue using extracellular vesicles that could be stored at room temperature, making it an off-the-shelf product that is easily accessible. If successful, this innovative therapy has the potential to revolutionize the treatment of corneal scars, greatly reducing the need for corneal transplants and eliminating the associated blinding complications, while improving access to care.

We appreciate the consideration of the CIRM ICOC for funding our TRAN1 application.

Sincerely,



Sophie X. Deng, M.D., Ph.D.  
Professor  
Joan and Jerome Snyder Chair in Cornea Diseases  
Co-Chief, Cornea and Uveitis Division  
Vice Chair, Justice, Equity, Diversity and Inclusion