The cornea is the primary lens in the eye and is the first line of defense for environmental and infectious insults. Corneal damage is often caused by mechanical, thermal, chemical, microbial, and radiation insults in the explosive conditions faced by soldiers. Severe corneal injuries with corneal epithelial stem cell deficiency are sight-threatening and often cause blindness. Corneal epithelial stem cell deficiency is also caused by ocular surface diseases such as Stevens-Johnson syndrome and inherited disorders such as aniridia. This is one of the most common blinding eye conditions worldwide and one of the most problematic conditions faced by ophthalmologists. Insufficiency of donor cornea for transplantation is critical around the world. Traditional penetrating corneal transplantation for treatment of these disorders generally produces dismal results with immunologic rejection, opacification, and ulceration of the cornea.

The potential of limbal stem cell transplantation for treating these conditions has recently been recognized. Grafting viable limbal tissue with its resident stem cell population may replenish the limbal stem cells and can restore a normal corneal epithelium. The success of limbal transplantation has been attributed to the healing potential of the limbal stem cells that are only a small population of cells contained within the mixture of cells that are transplanted in these limbal grafts. Thus, the longevity of these transplanted limbal epithelial cells remains a major concern because the whole population of limbal epithelial cells may not contain a sufficient number of viable stem cells for long-term maintenance of corneal epithelia. Although isolation of corneal epithelial stem cells has not been achieved due to lack of definitive markers to identify them, we have isolated clonogenic populations of human limbal epithelial progenitor cells (LEPC) based on a unique limbal basal cell phenotype. The LEPC have shown some properties that are characteristic of adult stem cells. These stem-like properties, especially the high proliferative potential and capability of regenerating a normal corneal epithelium ex vivo, suggest that the LEPC may represent the best cell source identified so far for use in corneal tissue engineering. We hypothesize that the stem cell-based corneal constructs can be bioengineered using human limbal epithelial progenitor cells for therapeutic repair of corneal injury.

Developing stem cell-based corneal tissue engineering using human LEPC would represent a breakthrough in this field. Fabrication of bioengineered corneal constructs will require novel approaches to isolate the LEPC, expand them in a suitable environment and deliver them to recipients using methods that meet the requirements of the US FDA. Three specific aims are proposed to fulfill this long-term objective: (1) To isolate sufficient human LEPC for use in corneal tissue bioengineering based on their unique basal cell phenotype; (2) To develop niche culture systems for ex vivo expansion of the isolated human LEPC; (3) To bioengineer new stem cell-based corneal constructs using LEPC grown on an optically transparent natural corneal stroma, which simulates native human corneal structures.

This procedure will permit coverage of the entire recipient cornea with a small number of donor LEPC that contain viable stem cells and will lead to a new generation of native-like corneal constructs engineered with stem cell-enriched LEPC, which will benefit patients with severe corneal injuries by restoring vision. These bioengineered new corneal constructs will facilitate future clinical trials for therapeutic repair of corneal injury or disease-damaged ocular surface. The potential clinical impact of using LEPC for
corneal reconstruction is enormous. Isolation of stem cell-containing LEPC would also facilitate the identification and isolation of putative limbal stem cells. This work will have important scientific significance and high impact in support of the adult stem cell concept, not only for cornea and ocular surface, but also for other tissues.