Induction of Corneal Endothelial Cells

Tech ID: 27338 / UC Case 2016-284-0

CONTACT

University of California, San Diego
Office of Innovation and Commercialization
innovation@ucsd.edu
tel: 858.534.5815.

OTHER INFORMATION

KEYWORDS

pluripotent stem cell, corneal endothelial cell, neural crest, eye field, small molecule, cornea, corneal endothelial dystrophy

CATEGORIZED AS

- **Medical**
  - Disease: Ophthalmology and Optometry
  - Stem Cell

RELATED CASES

2016-284-0

BACKGROUND

Ocular degenerative diseases including age-related macular degeneration (AMD), retinitis pigmentosa, glaucoma, and corneal endothelial dystrophy (CED) cause irreversible vision loss and affect millions of people worldwide. Currently, there is no effective drug intervention. Grafting healthy eye cells to replenish the diseased tissues such as retina represents a promising therapeutic approach. However, previous attempts at using primary human eye cells have met with limited success due to the limited expansion capacity and differentiation potential of adult progenitors or difficulty of obtaining sufficient human fetal retinal progenitors, and possible ethical concerns. Human pluripotent stem cells (PSCs), including human embryonic stem cells (ESCs), and induced pluripotent stem cells (iPSCs) represent promising renewable donor sources for cell-based replacement therapy. Nevertheless, PSCs themselves are not suitable for direct transplantation in clinical applications due to their tendency to form teratomas and low efficiency in repopulating host tissues with desirable reprogrammed cell types in vivo.

While the advancement of clinical trials of hESC-derived RPE transplants for treatment of patients with Stargardt's macular dystrophy and AMD is encouraging to the field, there is a great need for methods of generating unlimited other specialized eye cells effectively in vitro for treating blindness due to the loss of photoreceptors, RGCs and CECs. Therefore, there is a major interest in development of *in vitro* expandable cell sources for engineering corneal endothelium.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have developed a small molecule based methodology to derive human CESs from PSCs via ocular lineage specification. A three-step strategy was employed; [1] eye field stem cells (EFSCs) were derived from PSCs, (2) EFSCs were directed to ocular neural crest stem cells (NCSC) fate, and (3) differentiated ocular NCSCs to human corneal endothelial cells (CECs) resulting in a homogeneous and expandable monolayer of CECs in culture.

APPLICATIONS

- A therapeutic composition and method for treating a patient in need of ocular therapy.
- A research tool comprising a feeder-free and serum-free culture of corneal endothelial cells (CECs).
- A method of identifying a pharmaceutically active agent, comprising combining a pharmaceutical candidate with a feeder-free and serum-free culture of corneal endothelial cells (CECs) and detecting a desired pharmaceutical activity, thereby identifying a pharmaceutically active agent.

ADVANTAGES

Unlike previously reported induction procedures, the present methods utilize a novel small molecule-based approach to derive human CECs along with three major retinal cell types, RPE, photoreceptor and RGC, from PSCs in a directional fate restriction fashion. Moreover, using EFSC-derived NCSCs as a starting cell source cell, CECs can be quickly and directly induced and expanded in culture.

STATE OF DEVELOPMENT

The current methodology provides a research tool for generating feeder and serum-free culture of CDCs. The majority of CECs expressed ZO-1, N-cadherin and Na+/K+ATPase, all characteristic markers of CECs.

INTELLECTUAL PROPERTY INFO

Patent-pending. Worldwide rights are available.

RELATED MATERIALS

- Jiagang J. Zhao and Natalie A. Afshari. Generation of Human Corneal Endothelial Cells via In Vitro Ocular Lineage Restriction of Pluripotent Stem Cells. Invest Ophthalmol Vis Sci. 2016 Dec - 12/01/2016

PATENT STATUS

Country	Type	Number	Dated	Case
Patent Cooperation Treaty	Published Application	2017190136	11/02/2017	2016-284

University of California, San Diego

Office of Innovation and Commercialization

9500 Gilman Drive, MC 0910, ,

La Jolla,CA 92093-0910

Tel: 858.534.5815

innovation@ucsd.edu

https://innovation.ucsd.edu

Fax: 858.534.7345