

VISION SCIENCE AND EYE

August 10-11, 2017 | London, UK

The ubiquitin proteasome pathway in Cultured Oral Mucosa Epithelial Cell Sheet (CAOMECS) for ocular surface reconstruction

Fawzia Bardag-Gorce, Joan Oliva, Richard H. Hoft and Yutaka Niihara
Los Angeles biomedical research Institute, USA

Purpose: This study focuses on characterizing proteasomes in corneal epithelial cells (CEC) and in cultured autologous oral mucosal epithelial cell sheets (CAOMECS) used to regenerate the ocular surface.

Methods: Limbal stem cell deficiency (LSCD) was surgically induced in rabbit corneas. CAOMECS was engineered and grafted onto corneas with LSCD to regenerate the ocular surface. **RESULTS:** LSCD caused an increase in inflammatory cells in the ocular surface, an increase in the formation of immunoproteasomes (IPR), and a decrease in the formation of constitutive proteasome (CPR). Specifically, LSCD-diseased CEC (D-CEC) showed a decrease in the CPR chymotrypsin-like, trypsin-like and caspase-like activities while healthy CEC (H-CEC) and CAOMECS showed higher activities. Quantitative analysis of IPR inducible subunit (B5i, B2i, and B1i) were performed and compared to CPR subunit (B5, B2, and B1) levels. Results showed that ratios B5i/B5, B2i/B2 and B1i/B1 were higher in D-CEC, indicating that D-CEC had approximately a two-fold increase in the amount of IPR compared to CAOMECS and H-CEC. Histological analysis demonstrated that CAOMECS-grafted corneas had a re-epithelialized surface, positive staining for CPR subunits, and weak staining for IPR subunits. In addition, digital quantitative measurement of fluorescent intensity showed that the CPR B5 subunit was significantly more expressed in CAOMECS-grafted corneas compared to non-grafted corneas with LSCD.

Conclusion: CAOMECS grafting successfully replaced the D-CEC with oral mucosal epithelial cells with higher levels of CPR. The increase in constitutive proteasome activity is possibly responsible for the recovery and improvement in the treated corneas. Supported by Emmaus Life Sciences Inc.

Biography

Fawzia Bardag-Gorce has been studying ocular surface disease for the last six years, and has published and co authored six peer-reviewed publications in this field. She began her research on the treatment of limbal stem cell deficiency using Cultured Autologous Oral Mucosa Epithelial Cell Sheet (CAOMECS). During these six years, and under her supervision and guidance, her lab has successfully completed pre-clinical studies related to the efficacy and safety of CAOMECS cell-based therapy. She is currently directing a new study approved by the Institutional Research Board in which subjects are being recruited for the human oral mucosal epithelial cell sheet characterization. The long-term goal of this study is to regenerate corneal epithelium in patient with severe ocular surface diseases using autologous oral mucosa epithelial cell sheet grafts.

fgorce@labiomed.org

Notes: