Fawzia Bardag-Gorce et al., J Clin Exp Ophthalmol 2018, Volume 9
DOI: 10.4172/2155-9570-C5-090

Expression of ALDH in cultured autologous oral mucosal epithelial cell sheet (CAOMECS) grafts for ocular surface reconstruction

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Statement of the Problem: The transplantation of allogenic limbal epithelium in the form of a keratolimbal allograft from cadaveric tissue is one of the current treatments for patients suffering from injury to the ocular surface. However, transplantation of donor corneal tissue is dependent on the available supply, and the shortage of donor eyes is a well-known continuing problem worldwide. The use of allogeneic limbal grafts is not regarded as standard treatment; it requires systemic immunosuppression and has a poor rate of success. Recently, we have used a cultured non-limbal autologous cell type (Cultured autologous oral mucosa epithelial cell sheet or CAOMECS) to treat ocular surface disease (limbal stem cell deficiency or LSCD).

Aim: The purpose of this study is to focus on the expression of aldehyde dehydrogenases (ALDH1A1 and ALDH3A1) in CAOMECS. These enzymes reduce the levels of acetaldehyde, a highly reactive chemical that causes alterations in proteins and DNA. ALDH also protects against UV induced-oxidative damage and plays an important role in reducing ocular diseases associated with photophobia.

Methodology & Theoretical Orientation: To create LSCD, rabbits underwent surgical limbectomy. Rabbit oral mucosal epithelial cells were isolated and cultured to produce CAOMECS grafts. Microarray analysis profiling gene expression was used to detect gene expression of ALDH in cultured oral mucosal epithelial cells. Immunofluorescent staining and western blot analysis were used to examine ALDH protein levels in healthy and LSCD-diseased rabbit corneal epithelial cells.

Findings: Immunofluorescent staining showed that ALDH1A1 was highly expressed in healthy corneal epithelial cells. Staining of corneal epithelial cells in rabbits with LSCD showed greatly reduced expression. Western blot analysis confirmed the decrease of ALDH1A1 in LSCD-diseased corneal epithelial cells. Microarray analysis showed significant gene expression of exclusively ALDH1A1 in rabbit CAOMECS. Other investigators have shown that rabbit do not express ALDH3A1 in corneal tissue. Our data showed similar pattern in CAOMECS. The up regulated gene expression of ALDH1A1 suggests CAOMECS may have cytoprotective characteristics against ultraviolet radiation as well as oxidative damage.

Conclusion & Significance: These findings support the hypothesis that CAOMECS may protect against photophobia by grafting cells that contain ALDH, which may improve corneal epithelium cell function and corneal transparency.

Biography

Fawzia Bardag-Gorce has been studying Ocular Surface Disease for the last six years, and has since published and co authored six peer-reviewed publications in the 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.

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