AB089. Impact of WNK1 inhibition on corneal wound healing using a model of human tissue-engineered cornea

Pascale Desjardins[1,2], Camille Couture[1,2], Karine Zaniolo[1], Lucie Germain[1,2], Sylvain Guérin[1]

[1]Département d'ophtalmologie, CUO-recherche/LOEX, [2]Département de chirurgie, Centre de recherche en organogénèse expérimentale de l'Université Laval/LOEX, Centre de recherche du CHU de Québec, Université Laval, Québec, QC, Canada

Background: Because of its superficial anatomical localization, the cornea is particularly vulnerable to abrasive forces and various traumas, which can lead to significant visual impairments. Upon injury of the corneal epithelium, there are important changes that occur in the composition of the underlying extracellular matrix (ECM). Those changes are perceived by the integrins that recognize the ECM components as their ligand and activate different intracellular signalling pathways, ultimately leading to reepithelialisation and reorganization of the injured epithelium, both of which are necessary in order to restore the visual properties of the cornea. The goal of this study was to analyse the impact of the pharmacological inhibition of specific signal transduction mediators of integrin-dependant signalling pathways on corneal wound healing using both monolayers of hCECs and tissue-engineered human corneas (hTECs) as *in vitro* models.

Methods: hTECs were produced by the self-assembly approach and wounded with a 8-mm diameter biopsy punch. Total RNA and proteins were isolated from the wounded and unwounded hTECs to conduct gene profiling analyses and protein kinase arrays. The wounded tissues were then incubated with the WNK1 inhibitor WNK463 and wound healing was monitored over a period of 6 days. Control corneas were incubated with the vehicle alone (DMSO). The impact of WNK1 inhibition on hCECs monolayers was determined using a scratch wound assay.

Results: Gene profiling analyses and protein kinases arrays revealed important alterations in the expression and activity of several mediators from the integrin-dependent signalling pathways in response to the ECM changes taking place during corneal wound healing. Among these, WNK1 is considerably activated through phosphorylation during corneal wound healing. The pharmacological inhibition of WNK1 by WNK463 significantly reduced the dynamic of corneal wound closure in our hTECs and hCECs monolayers compared to their respective negative controls.

Conclusions: These results allowed the identification of WNK1 kinase as an important player for a proper healing of the cornea. Also, these results allowed for a better understanding of the cellular and molecular mechanisms involved in corneal wound healing and they may lead to the identification of new therapeutic targets in the field of corneal wounds.

Keywords: Cornea; tissue engineering; wound healing; signaling pathways; integrins

doi: 10.21037/aes.2018.AB089

Cite this abstract as: Desjardins P, Couture C, Zaniolo K, Germain L, Guérin S. Impact of WNK1 inhibition on corneal wound healing using a model of human tissue-engineered cornea. Ann Eye Sci 2018;3:AB089.