AB087. Corneal phenotype of a Slc4a11 knockout murine model for congenital hereditary endothelial dystrophy

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Background: Congenital hereditary endothelial dystrophy (CHED) is characterized by blindness at birth or in early infancy resulting from bilateral corneal opacification, and is linked to mutation in the Slc4a11 gene. A Slc4a11 knockout (KO) mouse, generated by gene deletion (Vithana *et al.* Nat Genet 2006), was acquired in order to study this disease. To confirm the phenotype of this Slc4a11 KO mouse model as a function of age, using the wild type (WT) mouse as a control.

Methods: Genotyping was performed by PCR (REDExtract-N-AmpTM Tissue PCR Kit, Sigma-Aldrich, Oakville, ON). Slc4a11 WT and KO mice populations aged from 5 to 50 weeks were studied (n=5 animals per age group; 5-year age intervals). Slit lamp examination, anterior segment-ocular coherence tomography (OCT930SR; Thorlabs, Inc., Newton, NJ), corneal endothelial cell staining, and scanning (SEM) and transmission (TEM) electron microscopy were used to assess the morphological and cellular differences between the two groups. The expression of basolateral membrane transporter NaBC1 within the corneal endothelium was also assessed using immunohistochemistry.

Results: Diffuse and progressive corneal opacification was observed at the slit lamp in the Slc4a11 KO mice, starting at 10 weeks. The central corneal thickness (CCT) also increased progressively as a function of time. In comparison, Slc4a11 WT corneas remained clear over the entire study period. Early TEM results showed vacuole degeneration of the corneal endothelium in the 15-week KO mouse, which was not seen in the same age WT mouse.

Conclusions: The corneal phenotype of this Slc4a11 KO mouse is representative of the clinical manifestations of CHED in human subjects, confirming the usefulness of this model for studying pathophysiology and therapeutic alternatives for Slc4a11-associated corneal dystrophies.

Keywords: Slc4a11; mouse; congenital hereditary endothelial dystrophy (CHED)

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