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Translational research shows promise for treating corneal endothelial disease

Using donor cornea tissue, whether full- or partial-thickness, is the mainstay for treating corneal endothelial disease, but new, innovative options in development are less invasive and could provide better outcomes. **Shigeru Kinoshita, MD, PhD**, Kyoto, Japan, described 2 "out of the box" approaches he has taken to treat corneal disease in his presentation, "Future Directions in Corneal Endothelial Cell Biology," the keynote lecture at Friday's "Corneal Tissue Engineering, Physiology, and Wound Healing" session.

One of the options Dr. Kinoshita has begun to explore is injecting cultivated corneal endothelial cells (CECs) from a donor cornea for advanced-stage diseases such as Fuchs' endothelial corneal dystrophy (FECD) or pseudophakic bullous keratopathy (BK). In addition to being less invasive than an endothelial keratoplasty, this technique helps conserve precious donor tissue—1 donor cornea can provide enough cells to treat more than 200 patients.

The surgical procedure involves removing the pathologic endothelium, aspirating the aqueous humor, pumping in rho-kinase (ROCK) inhibitors, and injecting a suspension of 1 million CECs. After the procedure, the patient must remain face down for 3 hours to allow the cells to adhere to Descemet's membrane.

After initial success in animal models, Dr. Kinoshita began culturing cells for use in the clinic. So far, he has injected CECs into 11 patients with either FECD or BK and has achieved excellent visual outcomes. One patient with FECD he treated had a preop BCVA of 20/400 and a central corneal thickness of 778 µm, but after CEC injection, had a BCVA of 20/20 and a central corneal thickness of 525 µm.

For early phase endothelial disease, Dr. Kinoshita has been developing a method of using ROCK inhibitor eye drops to stimulate recovery of a patient's endothelial function. ROCK inhibitors promote cell adhesion and proliferation and inhibit apoptosis, making them excellent candidates for this procedure.

In the eye drop procedure, Dr. Kinoshita uses transcorneal freezing to induce a partial endothelial defect in the patient's central cornea and then applies the ROCK inhibitor drops 6 times daily for 7 days. The patient's peripheral endothelial cells then migrate to the center of the cornea and repopulate the lost cells.

Using a rabbit model, Dr. Kinoshita showed that ROCK inhibitors promoted wound healing and closed the endothelial defect in 48 hours. Dr. Kinoshita then successfully performed the procedure on a 52-year-old patient with FECD. Three years after the treatment, the patient had a BCVA of 20/20 and central corneal thickness of 568 µm.

The ROCK inhibitor eye drop method works well for treating central endothelial defects and edema, such as FECD, but not well for diffuse edema from BK, Dr. Kinoshita said. He has also worked on elucidating the molecular mechanisms behind ROCK activity, showing that ROCK inhibition increases cell proliferation by controlling the G1/S transition, the “point of no return” in the cell cycle that forces it to divide.

Using CECs and eye drop therapy allows physicians to treat disease at an earlier stage and offer a less invasive alternative to a corneal transplant. It is his hope, Dr. Kinoshita said, that this translational research will promote the development of even more novel therapies for the treatment of corneal endothelial diseases. As these methods embody the shift from highly invasive to minimally invasive procedures, Dr. Kinoshita believes they represent the future of corneal endothelial dysfunction treatment.