

# News in Review

COMMENTARY AND PERSPECTIVE

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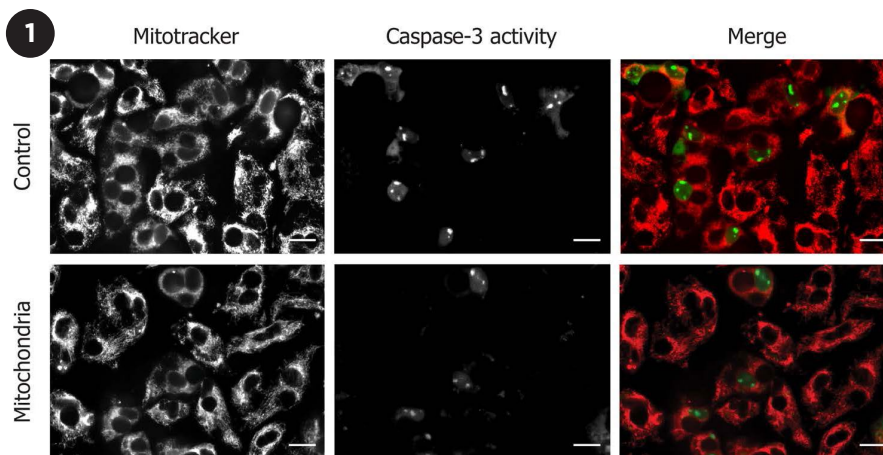
## Mitochondria Infusion May Slow Fuchs

**IN A PROOF-OF-CONCEPT STUDY,** Canadian researchers showed that incorporation of healthy mitochondria into corneal endothelial cells from Fuchs dystrophy patients could reverse some traits of the affected cells and delay progression of the disease.<sup>1</sup> Although still at the preclinical stage, this mitochondrial transplantation could eliminate the need for corneal transplants in Fuchs patients.

**The need for new treatment.** Currently, corneal tissue transplantation is the only established curative treatment available to prevent the loss of endothelial cells and maintain corneal transparency in Fuchs eyes. However, the limited availability of donor corneas in many parts of the world and risk of rejection are common challenges with corneal transplantation.

Despite mounting evidence of the important role of mitochondria in Fuchs pathogenesis, limited efforts have been made until now to treat Fuchs by directly targeting the mitochondria, said Patrick J. Rochette, PhD, at Université Laval in Québec City. “Our findings do suggest that internalization of healthy mitochondria in corneal endothelial explants from patients with Fuchs could rescue cellular function and slow the loss of endothelial cells,” he said.

**The methodology.** The team ob-

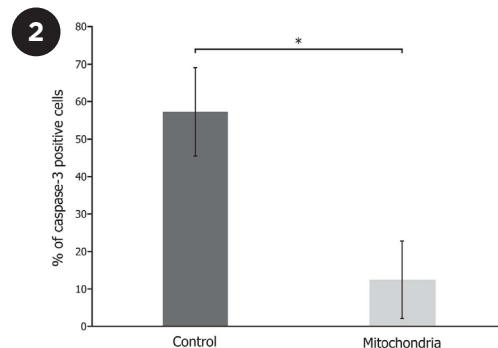


**FUCHS.** (1) An apoptosis marker (green) and a mitochondrial mass marker (red) in Fuchs explants with and without exogenous mitochondria. Scale bar = 40  $\mu$ m. (2) The number of apoptotic cells is fewer in the explants treated with mitochondria than in controls.

tained corneal endothelium explants isolated from patients with late-stage Fuchs dystrophy. To determine the potential therapeutic effects of mitochondrial transplantation, they co-incubated these corneal explants with functional mitochondria isolated from healthy cultured cells. The team then assessed the efficiency of exogenous mitochondrial incorporation and its effects on cellular function and phenotypes.

**Changes in pathological markers.** The results showed that a three-hour co-incubation was sufficient for Fuchs cells to incorporate the healthy mitochondria. Internalization of the functional mitochondria into these cells increased mitochondrial membrane potential and energy production while reducing mitophagy and oxidative stress.

“These findings confirm that Fuchs cells can internalize exogenous mito-



chondria after co-incubation and that incorporation of healthy mitochondria reverses several cellular phenotypes of the disease that contribute to Fuchs progression,” said Dr. Rochette.

**A novel finding.** Programmed cell death has long been considered an irreversible process in Fuchs, said Dr. Rochette, and the endothelial cell depletion and subsequent energy imbalance caused by apoptosis initiates a cycle promoting further disease progression. So, he said, it was a surprise when the team found that internalization of healthy mitochondria in Fuchs cells significantly reduced apoptosis. “The fact that the incorporation of exogenous mitochondria could reverse this apoptosis in cells from patients with late-stage Fuchs suggested that our approach could help break this vicious cycle,” he added.

**Looking ahead.** The team plans to further investigate the feasibility of its

approach using in vivo models before moving to clinical trials to evaluate the safety and efficacy of the method in humans. However, the early results do suggest an entirely new avenue of treating Fuchs, said Dr. Rochette.

—Christos Evangelou, PhD

1 Méthot S et al. *Sci Rep.* 2023;13(1):3380.

Relevant financial disclosures: Dr. Rochette—None.

## COMPREHENSIVE

# Eyedrop Bottle Adaptor May Make Drops Last Longer

**EYEDROP BOTTLES EQUIPPED WITH** a novel adaptor proved effective in delivering smaller drops than bottles with a stock bottle tip.<sup>1</sup> The Nanodropper (Nanodropper) also increased the total number of drops per bottle, thereby theoretically extending the life of a one-month supply to around 2.5 months.

“There are real limitations to the way we deliver ophthalmic medications with standard eyedrop bottles,” said Leonard K. Seibold, MD, at the University of Colorado School of Medicine in Aurora. Some patients run out of drops too soon, have trouble affording drops, or experience excessive side effects. “These issues can collectively lead to poor adherence, which in turn can lead to poor outcomes and even vision loss,

in the case of glaucoma. One way to alleviate some of these issues is through the consistent delivery of smaller eye-drops with less waste, while prolonging the life of a bottle. The Nanodropper bottle adaptor is one way to achieve this.”

**Adaptor versus standard drop volume.** In this experimental study, the team tested the volume-reducing adaptor, which twists onto a compatible stock bottle, on nine ophthalmic medications: six topical ocular hypotensive drugs, one steroid, and two artificial tears emulsions. They determined average drop volume and total number of dispensed drops from bottles with and without the Nanodropper. The adaptor decreased drop volume by an average of 62.1%. Mean drop volume was  $39.8 \pm 2.1 \mu\text{L}$  for stock bottles versus  $15.1 \pm 1.0 \mu\text{L}$  for the Nanodropper. What’s more, the adaptor delivered 2.6 times the total number of drops per bottle for all medications. Stock bottles of 2.5 mL dispensed a mean of  $69.8 \pm 4.9$  drops compared with  $184.1 \pm 15.1$  drops with the adaptor. The adaptor was similarly effective for solutions, suspensions, and emulsions.

**Ideal drop volume still unknown.** Despite these robust findings, the study did not provide data on the efficacy of smaller drops. Clinical trials will have to address that issue, said Dr. Seibold. “However, when you consider the limited volume of the tear film and conjunctival cul-de-sac, it is likely that drop volume greater than 20  $\mu\text{L}$



**ADAPTOR TIP.** Placed on a stock bottle, a specialized adaptor tip delivers more and smaller drops.

provides no real additional benefit.” He said this may explain why drops almost always roll down the cheek, no matter how accurately they are placed.

Clinical trials will also be necessary to address patient adherence and satisfaction with the adaptor, as well as IOP-lowering efficacy in patients with ocular hypertension and glaucoma, and cost analyses for medication use with and without the adaptor, he said.

**A potential bonus.** While the issue of medical waste was not part of the study, Dr. Seibold noted that by reducing the amount of medicine lost with each drop applied, the Nanodropper may theoretically reduce medical waste by more than 50%. —Miriam Karmel

1 St. Peter DM et al. *Med Devices: Evid Res.* 2023; 16:71-79.

Relevant financial disclosures—Dr. Seibold: None.

## NEURO-OPHTHALMOLOGY

# Few Neuro-Ophthalmic Articles in Influential Journals

**ALTHOUGH NEURO-OPHTHALMOLOGY IS AN ACADEMIC-**oriented subspecialty, a recent study shows that it is underrepresented in influential ophthalmology and neurology journals, in both original research and literature reviews as well as editorial board expertise.<sup>1</sup>

Edward Margolin, MD, a study coauthor at the University of Toronto in Toronto, Ontario, said the findings suggest that editorial priorities could be influencing the disproportionate publication of neuro-ophthalmology articles. Moreover, he stressed that neuro-ophthalmic research dissemination among general ophthalmologists and neurologists is crucial because of the limited

number of highly qualified medical providers in the extremely specialized and complex field of neuro-ophthalmology. “At least 10% to 15% of patients seen in general ophthalmology practices will present with a problem that is relevant to neuro-ophthalmic knowledge,” said Dr. Margolin. “Practitioners must be educated in these types of disease to best support prompt diagnosis and treatment.”

**A look at the literature.** The researchers evaluated 10 ophthalmology and neurology journals, five in each specialty, over the last decade. Journals were selected for their high “impact factor,” the rate at which the average journal article is referenced in a specific time frame.

A total of 104,558 articles were categorized as either “neuro-ophthalmology focused” or “other.” Each article was also classified as “teaching” or “nonteaching,” the latter of which included original research and literature

reviews. Editors from each of the journals were identified and designated as “neuro-ophthalmologists” or “non-neuro-ophthalmologists” based on their medical training and clinical practice.

The researchers then used descriptive statistics to determine the proportion of neuro-ophthalmology articles published in each journal every year across the 10-year span. In addition, they used correlation analysis to identify relationships between editorial board representation and publication frequency for teaching and nonteaching articles with a neuro-ophthalmology focus.

**Publication trends.** Across all 10 journals, only 3.4% of the published content consisted of nonteaching neuro-ophthalmology articles, and only 1% to 7% of the editorial seats from each board were filled with neuro-ophthalmologists. Correlation analysis of the data also revealed that increased neuro-ophthalmology presence and expertise on editorial boards correlated with increased publication of neuro-ophthalmic teaching articles.

**A caveat.** A limitation of the study, the authors wrote, is that they were unable to assess “a comparison dataset of articles”—submissions rejected during the editorial or peer review processes. Those data are not publicly available, they noted. This information might have helped to give a sense of the relative proportion of papers received that went on to be published and, perhaps, some insight into the selection process.

**Call for more published research.** High-impact medical journals naturally seek out submissions that will appeal to their readers, resulting in more widely read and cited articles, Dr. Margolin said. However, he is concerned that the underrepresentation of published neuro-ophthalmic research within influential neurology and ophthalmology journals may hinder the widespread communication of knowledge that could benefit practitioners who treat patients with these less-common disorders.

He suggested that editors may unknowingly be drawn toward submissions covering familiar subject matter sent from institutions with which they already have strong relationships. Conversely, they may shy away from articles that appear irrelevant to the bulk of their readership or are submitted by lesser-known researchers. Even so, said Dr. Margolin, it is important to address this apparent publication disparity and promote more neuro-ophthalmology research in high-impact journals. —Julie Monroe

1 Xie J et al. *Can J Ophthalmol*. Published online April 8, 2023.

**Relevant financial disclosures**—Dr. Margolin: None.

See the financial disclosure key, page 10. For full disclosures, view this News in Review at [aao.org/eyenet](http://aao.org/eyenet).

## IMPORTANT PRODUCT INFORMATION

### ARGOS® Optical Biometer

**Caution:** Federal (USA) law restricts this device to the sale by or on the order of a physician.

**Indications:** ARGOS® is a non-invasive, non-contact biometer based on swept-source optical coherence tomography (SS-OCT). The device is intended to acquire ocular measurements as well as perform calculations to determine the appropriate intraocular lens (IOL) power and type for implantation during intraocular lens placement.

**Intended Use:** The Reference Image functionality is intended for use as a preoperative and postoperative image capture tool. It is intended for use by ophthalmologists, physicians, and other eye-care professionals and may only be used under the supervision of a physician.

### Warnings and Precautions:

- Only properly trained personnel with experience may operate the device and control software and interpret the results.
- Factors that influence the measurement of patient's eyes are listed in the User Manual (Table 1): pseudophakic eye, wearing contact lenses, fixation problem, cornea opacity, non-intact cornea, refractive surgery, blood in the vitreous humor, retinal detachment, keratoconus, asteroid hyalosis, ambient light in the room, and deformation of the corneal shape. Please consider the guidance provided in Table 1 when you encounter these factors.
- Optical Radiation - This device is equipped with a Class 1 laser light source.

**ATTENTION:** Refer to the ARGOS® User Manual for a complete description of proper use and maintenance, optical and technical specifications, as well as a complete list of warnings and precautions.

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