Fuchs' endothelial corneal dystrophy:

Heredity behind common corneal disease

On October 15, 2021, Andreas Viberg defended his thesis "Fuchs' endothelial corneal dystrophy—Genetic etiology and as a risk factor in cataract surgery" at the Department of Clinical Sciences, Ophthalmology, Umeå University. The PhD project was supervised by Berit Byström, MD, PhD, Department of Clinical Sciences, Ophthalmology, with co-supervisors Irina Golovleva, PhD, Department of Medical Biosciences/Medical and Clinical Genetics and Patrik Danielson, MD, PhD, Department of Integrative Medical Biology, Anatomy, Umeå University, Sweden.

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Key points:

- FECD is associated with $(CTG)_n$ expansion in *TCF4*, and repeat length is associated with disease severity.
- Patients with cataract and concomitant corneal guttata benefit from cataract surgery, but corneal guttata is associated with inferior results in both visual acuity and patient self-assessed visual function.

Nine out of ten of those with a common corneal disease have rare genetic changes. The findings of this dissertation may be important for the choice of treatment, which often includes corneal transplantation.

Fuchs' endothelial corneal dystrophy (FECD) causes visual impairment and pain. The hallmarks of FECD include corneal guttata, which is the excessive accumulation of extracellular matrix in the corneal endothelial basement membrane and the loss of endothelial cell function. In order to develop new treatment strategies that increase the patient's quality of life, it is valuable to understand the disease mechanisms. Although the disease affects only around 4% of the population, it is the most common cause of corneal transplantation in Sweden and many other countries.

The first portion of this dissertation studied the genetic cause of FECD by looking at 102 cases and an equally large healthy control group. Of the patients studied, 90% had changes in the gene *TCF4*. The change, which consisted of an increased number of repetitions of a specific DNA sequence, was only seen in 4% of the general population. There was also a connection between the repetition length of the DNA sequence and the severity of the disease.

The second part of the dissertation studied the outcome of cataract surgery in patients with both cataracts and FECD. This study was based on quality registers from the Swedish national cataract registry and the Swedish cornea transplant registry with several thousand people. The results suggest that FECD patients benefit from cataract surgery, but, at the same time, they are at risk of poorer results than patients with only cataracts, and they have an increased risk of subsequent corneal transplantation.

Because it is not uncommon for visual problems to be caused by a combination of cataracts and FECD, I hope the results of this dissertation can be helpful in choosing treatment for these patients.

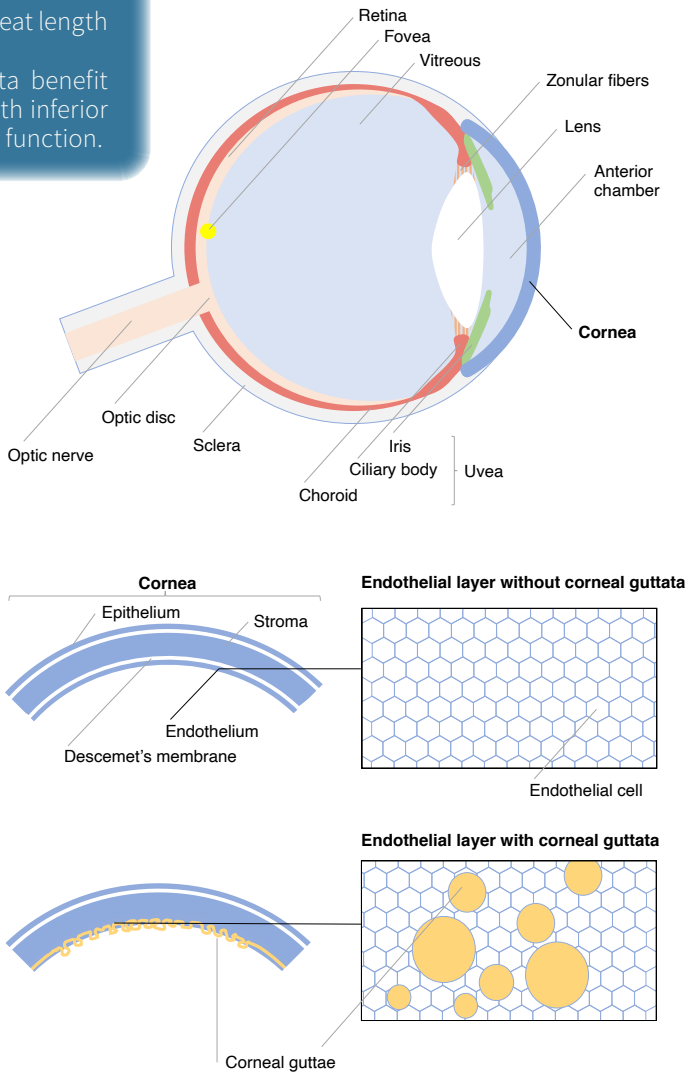

Figure 1. Basic eye anatomy and localization of the cornea (upper). The corneal layers (bottom left) and histological presentation of the hexagonal cells in the endothelial layer (bottom right), without and with corneal guttata (in orange). Illustrations by Andreas Viberg.

Remaining questions:

- Does a $(CTG)_n$ repeat expansion in *TCF4* impact cataract surgery results in patients with FECD?
- Can the development of a genetic test be useful in difficult cases?

References

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