**////Title: Understanding Myopia-26: A Rare Visual Disorder**

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Myopia – better known as short-sightedness – is a global health problem in which the eye grows too long, meaning it cannot produce clear images of objects in the distance. The common form of myopia is readily treated through the wearing of glasses, contact lenses or conducting laser surgery. It is also polygenic, meaning that many genes are likely to be involved in its inheritance through generations.

In contrast, certain rare forms of the disease start with severe short-sightedness in childhood, and ocular elongation tragically progresses to near complete blindness by the time the sufferer reaches middle age. These rare forms are usually controlled by just one single gene.

Dr Fehér at the Biological Research Centre in Szeged, Hungary, is working with Dr Széll and Dr Sohajda, ophthalmologists from the University of Debrecen, to better understand this rare but devastating class of visual disorders.

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Their consortium recently presented the first description of a Caucasian family afflicted by myopia-26. This rare form of the disease oddly affects females only, although males are obviously carriers.

The researchers conducted basic and detailed ophthalmological and electrophysiological examinations on a total of 18 family members. Curiously, while dysfunction of the central macula located in the centre of the retina in the eye was detected in both males and females, only females showed the symptoms of myopia.

The researchers carried out whole-exome sequencing of two family members to shed light on the genetic causes of this disease. They identified a mutation disrupting the ARR3 gene on the X-chromosome, consistent with the established literature of myopia-26.

The researchers developed two intriguing hypotheses to explain their key observations, based on electrophysiology findings and on the two primary cell types where ARR3 is normally expressed.

The first of these cells are known as pinealocytes, or cells of the pineal gland, the central endocrine organ controlling circadian rhythm. Decreased ARR3 function here may lead to a circadian rhythm defect, for example, a disturbed sleep-wake cycle, which is known to cause ocular elongation and myopia.

Cones are the second type of affected cell, the retinal cells responsible for coloured vision. Distinct cone types specifically sensing red, green and blue light have been identified. ARR3 is responsible for turning off or ending the activity of cones after being stimulated. The ARR3 defect primarily affects cones sensing green and red light, which results in the intensification of green/red impulses transmitted from the retina.

Due to the phenomenon of chromatic aberration, such altered impulses are equivalent to the case of image formation not in the plane of the retina, but behind it, an anomaly called hyperopic defocus. It is known from animal experiments that hyperopic defocus also leads to ocular elongation, therefore myopia, in due course.

Importantly, these two hypotheses are not mutually exclusive, and the researchers note that both may be working in parallel and/or in conjunction with further as of yet unspecified mechanisms.

In conclusion, Dr Fehér and his colleagues have shown that myopia-26 is not limited to the East Asian ethnicity as previously thought. Future research is required to better delineate the pathogenesis of the disorder, and in particular, explain why it is limited to females.