PRESS RELEASE

New Hereditary Retinal Disease Discovered

Night vision disrupted before visible retinal damage, while central vision remains relatively preserved

Chairman of the Management Board and Medical Director
Prof. Dr. Uwe Reuter, MBA
Tel: +49 228 287-10900
Fax: +49 228 287-9010900
Uwe.Reuter@ukbonn.de

Public Relations and Corporate Communication

Felix Heyder
Management

Tel.: +49 228 287-10469
felix.heyder@ukbonn.de

Bonn University Hospital
Venusberg Campus 1
Building 02
53127 Bonn

Bonn, September 10 – An international team of researchers led by the University Hospital (UKB) and University of Bonn, as well as the universities of Edinburgh, Basel and Pennsylvania, has identified a previously unrecognized form of inherited retinal degeneration caused by a specific variant in the *EFEMP1* gene. The disease primarily affects the peripheral retina and the rod photoreceptors responsible for vision in dim light and darkness. Importantly, rod function may already be severely impaired while the retina still appears largely normal on clinical examination. The results of the study have now been published in the journal *JAMA Ophthalmology*.

Working across centers in Edinburgh, Basel, Philadelphia, Prague and Bonn, the researchers studied three unrelated families carrying the same rare *EFEMP1* variant, p.Arg140Trp. Their findings establish this variant as the cause of a distinct, late-onset retinal degeneration that differs markedly from other diseases previously associated with *EFEMP1*.

“What made this discovery possible was bringing together observations that, in isolation, could easily have been interpreted as coincidental genetic variation. By combining genetic information across families with detailed clinical and experimental data, we were able to connect them to a single genetic cause and define a disease phenotype that had not previously been recognized as such,” says co-first author Chloe M. Stanton from the University of Edinburgh, who led the study together with co-first author Georg Ansari from the University of Basel. Laboratory experiments provided further clues as to why. The p.Arg140Trp form of the EFEMP1 protein accumulated unusually inside cells, showed an increased tendency to form abnormal molecular complexes, and was less efficiently secreted from cells.

Disease can begin before retinal damage is visible

The newly described disorder follows a distinctive pattern. Disease manifestations predominantly involve the responsible for perceiving the surroundings peripheral retina, which is responsible for perceiving the surroundings, while the central retina – including the area responsible for high-resolution vision – can remain relatively well preserved for many years. Early symptoms include difficulty seeing at dusk or in darkness and progressive loss of peripheral visual function. Because visual acuity may initially remain completely normal and routine examination of the retina can appear unremarkable, the disease may go undetected for a considerable period.

In several patients carrying the variant, researchers found markedly delayed recovery of rod-mediated vision after exposure to light despite normal visual acuity and an apparently normal retina. “One of the most striking findings is that retinal dysfunction clearly precedes visible structural degeneration,” says co-corresponding author Artur V. Cideciyan from the University of Pennsylvania. “We can detect a major abnormality in the way rod photoreceptors recover

in darkness at retinal locations that still look structurally intact. This gives us a functional marker of disease at a stage when photoreceptor cells have not yet been lost."

One gene, two strikingly different retinal diseases
EFEMP1 was already known to cause Doyne honeycomb retinal dystrophy/Malattia Leventinese, a rare inherited retinal condition historically associated with the Leventina Valley in Switzerland. However, the established form of Malattia Leventinese is caused by a different *EFEMP1* variant, p.Arg345Trp, and primarily affects the central retina. The newly characterized p.Arg140Trp variant affects the peripheral retina, while the macula – the central retinal region responsible for high-resolution vision – remains relatively preserved. The study therefore demonstrates that different variants within the same gene can result in strikingly different patterns of retinal disease.

"Previously, *EFEMP1* was strongly associated with a very characteristic central retinal phenotype. We now show that another variant in the same gene can produce a fundamentally different disease, with essentially an opposite disease pattern," says co-corresponding author Maximilian Pfau from the UKB, who also conducts research at the University of Bonn. "The newly described disease shares similarities with other rare inherited eye disorders including gyrate atrophy, choroideremia, extensive macular atrophy with pseudodrusen, and diffuse-trickling geographic atrophy, particularly at advanced stages. *EFEMP1* p.Arg140Trp-related disease may therefore account for eye disorders whose underlying genetic cause has so far remained unresolved."

The researchers caution that the present study includes only three unrelated families. Larger studies will be needed to determine the full clinical spectrum, natural history and frequency of the newly defined condition, and to assess potential therapeutic strategies.

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Scientific contact:
Prof. Dr. Maximilian Pfau
Senior Physician at the Department of Ophthalmology
University Hospital Bonn
Chair of Retinology and Hereditary Retinal Diseases
University of Bonn
Email: Maximilian.Pfau@ukbonn.de

Artur V. Cideciyan
University of Pennsylvania
Email: cideciya@pennmedicine.upenn.edu

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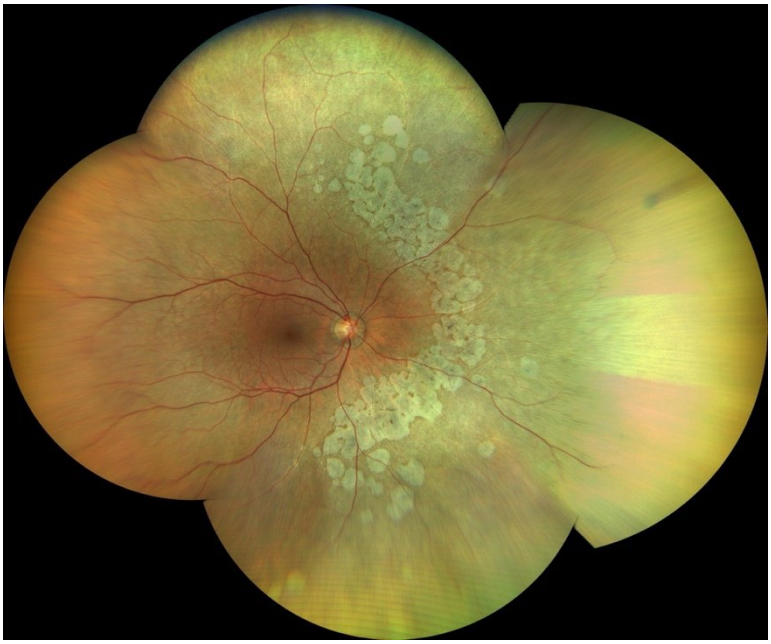

Caption: The Color fundus photograph shows the retina of a patient carrying the EFEMP1 p.Arg140Trp variant. The areas on the right correspond to regions of outer retinal degeneration. In contrast, the macula remains relatively preserved.

Picture credits: University Hospital Bonn (UKB) / Prof. Maximilian Pfau

Press contact:
Dr. Inka Väth
Deputy Press Officer at the University Hospital Bonn (UKB)
Public Relations and Corporate Communication at UKB
Phone: (+49) 228 287-10596
E-mail: inka.vaeth@ukbonn.de

About the University Hospital Bonn: As one of Germany's leading university hospitals, Bonn University Hospital (UKB) combines excellence in medical care and research with high-quality teaching. Every year, UKB treats more than half a million outpatients and inpatients. Around 3,500 students are enrolled in medicine and dentistry, and over 600 individuals receive training in healthcare professions annually. With around 9,900 employees, UKB is the third-largest employer in the Bonn/Rhein-Sieg region. In the „*Focus* hospital rankings", UKB is rated the top university hospital in North Rhine-Westphalia and has the second-highest case mix index (an indicator of treatment complexity) of all university hospitals nationwide. In 2025, UKB secured nearly €100 million in third-party funding for research, transfer, and teaching. For the fourth consecutive year, the F.A.Z. Institute recognized UKB as both "Germany's Training Champion" and "Germany's Most Desirable Employer." For current figures and further information, please refer to the annual report at: geschaeftsbericht.ukbonn.de