

Media Release

Finding the genome's blind spot

A long-missing genetic explanation for inherited vision loss

Basel, 9 January 2026 – Retinitis pigmentosa (RP) is a genetic eye disorder affecting around one in 5,000 people worldwide. It typically begins with night blindness in youth and progresses to tunnel vision as daylight-sensing photoreceptor cells in the retina gradually die, potentially leading to blindness over time. Although more than a hundred genes have been linked to RP, the genetic cause remains undiagnosed in ~30-40% of patients, even after extensive DNA testing. For many families, this has meant years without clear answers about their inherited vision loss.

That uncertainty is now beginning to lift: Researchers at the Institute of Molecular and Clinical Ophthalmology Basel (IOB), working with more than 100 institutions worldwide, analyzed genetic data from almost 5'000 individuals across 62 families affected by RP. The disease-causing changes were not found in protein-coding genes. In 153 patients, the researchers instead identified changes in RNA molecules involved in the cell's splicing machinery, which edits genetic information before proteins are made.

Key findings:

- **Variants in five non-coding RNA genes (RNU4-2, RNU6-1, RNU6-2, RNU6-8 and RNU6-9) cause retinitis pigmentosa.** These genes produce RNA molecules rather than proteins, representing a largely unexplored source of inherited blindness.
- **The variants are both inherited and spontaneous.** Some were passed down through generations; others appeared for the first time in affected individuals.
- **All variants cluster in the same critical region,** where the U4 and U6 RNA molecules, encoded by the RNU4 and RNU6 genes on the DNA, connect. This is a key interaction site for multiple proteins involved in RNA splicing.
- **One same gene can cause different diseases.** While certain variants in RNU4-2 lead to neurodevelopmental disorders, those identified here specifically target the retina.

This discovery solves a puzzle. While it was already known that some proteins involved in RNA splicing (PRPF3, PRPF8, and PRPF31) cause RP when mutated, this study reveals that the RNA molecules of the splicing machinery can also have disease-causing variants. In other words, multiple parts of the same cellular process, when broken, lead to the same condition.

For the families included in this study, the impact is concrete. These variants explain up to 1.4% of previously undiagnosed RP cases, which means that dozens of families worldwide can now receive a precise molecular diagnosis. They can access genetic counselling, make informed decisions about family planning, and position themselves for future treatments as they emerge.

More broadly, this study is an important step forward in the understanding of hereditary blindness. By looking beyond protein-coding genes into overlooked regions of the genome, researchers have expanded the diagnostic landscape. As genetic testing evolves and RNA-based therapies advance, these findings lay essential groundwork for identifying more patients and, ultimately, developing treatments for a disease that currently has no cure.

The full article, “*De novo and inherited dominant variants in U4 and U6 snRNA genes cause retinitis pigmentosa*” is available in *Nature Genetics* at <https://www.nature.com/articles/s41588-025-02451-4>

About IOB

At the Institute of Molecular and Clinical Ophthalmology Basel (IOB), basic researchers and clinicians work hand in hand to advance the understanding of vision and its diseases, and to develop new therapies for vision loss. IOB started its operations in 2018. The institute is constituted as a foundation, granting academic freedom to its scientists. Founding partners are the University Hospital Basel, the University of Basel and Novartis. The Canton of Basel-Stadt has granted the institute substantial financial support.

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