Institute of Molecular and Clinical Ophthalmology Basel

Media release

GENE THERAPY SENSITIZES RETINAS TO NEAR-INFRARED LIGHT
A new strategy for reversing vision loss from macular degeneration

BASEL SWITZERLAND, June 5, 2020

A team based at the Institute of Molecular and Clinical Ophthalmology Basel (IOB) has sensitized blind retinas to near-infrared (NIR) light. The NIR gene therapy, published today in *Science*, has the potential to improve vision in patients with macular degeneration.

Macular degeneration is a high-priority disease, causing significant vision loss in 200 million people worldwide. Patients retain peripheral eyesight but lose central vision over time. Though treatments may slow progression, current treatments are unable to bring back retinal light sensitivity.

"Restoring light sensitivity may ultimately increase quality of life and participation in daily activities. Enabling NIR light sensitivity allows maximum compatibility with remaining peripheral vision," says Botond Roska, Director at IOB, and one of the paper's corresponding authors.

“For macular degeneration, a wavelength is needed that functioning retinal cells are unable to see," says Dasha Nelidova, a postdoctoral fellow in the lab of Botond Roska, and the paper's first author. “Bright, visible light overwhelms the sensitive retinal periphery”. Patients with macular degeneration retain their peripheral eyesight, but lose central vision over time.

Inspired by infrared vision in snakes, IOB researchers developed a NIR light sensor based on gene therapy and nanotechnology. Ophthalmic gene therapy uses a mild, naturally occurring virus (AAV) as a vehicle to transfer genes to specific cells. Virally packaged genes and gold nanoparticles were delivered by subretinal injection, a technique requiring expertise in intraocular surgery.

Gold nanoparticles act as light antennas and absorb incoming NIR light. The gene equips retinal cells with heat-sensitive mammalian or reptile proteins (transient receptor potential (TRP) ion channels) to allow passage of ions from outside to inside the cell. As a result, NIR light induces nerve impulses in damaged retinal cells, similar to those generated when visible light is absorbed. In testing, NIR gene therapy generated at least partial vision in blind mice. Nerve impulses travelled from retinal cells via the optic nerve to visual processing areas in the brain. *Ex vivo* testing performed on human retinas collected from adult multiorgan donors confirmed the result.

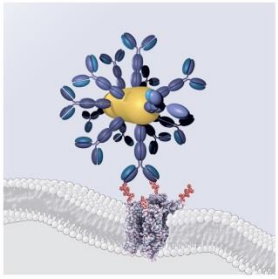
This new approach builds on ongoing efforts by IOB researchers and their collaborators in Paris to treat total blindness with optogenetic gene therapy. Optogenetics entails the delivery of visible spectrum-sensitive algae proteins to retinal cells and is in clinical trials for patients with no remaining vision. Patients wear eye goggles that project light patterns onto the retina. Eye goggles are also able to convert natural scenes to modified NIR images.

An approved gene therapy is available for patients with a rare form of inherited vision loss. Breakthrough approaches are also needed to treat the more common causes of blindness,

including macular degeneration. IOB researchers are in the early stages of developing a gene therapy that combines natural and NIR vision, giving hope that further development will enable improved visual function in patients with macular degeneration.

Original publication
Nelidova et al. (2020): Restoring light sensitivity using tunable near-infrared sensors. Science.

Illustration:
Print file for download:
https://iob.ch/fileadmin/generic_lib/Resources/Public/Downloads/Nelidova_1A_NIRsensor1.jpg



Caption:
Three-component system: Antibodies (blue), gold nanorod (gold) and heat-sensitive channel (structure in the membrane; below the antibody-gold nanorod-conjugate). Photo: Dasha Nelidova / IOB.ch

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. www.iob.ch

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