Inherited blindness is almost impossible to treat.
Now there is hope - even if the project of Matthias Steger's Swiss biotech company still sounds futuristic.

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Three of their four children will go blind in the course of their lives: the parents, Edith Lemay and Sébastien Pelletier, are trying to make the best of this sad fate. The family from Canada is currently traveling around the world so that their children can see and experience as much of it as possible.

As adults, three of these four children will go blind. The parents therefore travel around the world with them. Here they learn to surf in Bali.

Mia (12), Colin (7) and Laurent (5) suffer from the hereditary retinal disease retinitis pigmentosa, which causes gradual loss of sight. Only son Leo (9) has not inherited the disease. The family started out in Namibia, and in the meantime the children are learning to surf in Lombok, Indonesia, and visiting temples in Malaysia. The parents make the trip public on Instagram ("pleinleursyeux") and thus move around the world. The mother wants to fill their visual memory with the best and most beautiful pictures. Because, at the moment, their blindness cannot be averted.

The loss of eyesight

1 in 3000 people in Switzerland suffer from retinitis pigmentosa.
1.5 million people worldwide are affected by retinitis pigmentosa worldwide
80% of information about the outside world, is perceived via the sense of sight
⅓ of those aged 80 and older suffer from age-related macular degeneration
macular degeneration (AMD)

But there is hope: a clinical trial is currently underway in the United States for a novel drug that could halt and even reverse the genetically determined degeneration of the retina. Behind it is Matthias Steger (52) of Zurich, Switzerland, and his biotech company Endogena Therapeutics. **"The tragedy of this disease is that you know you're going blind, but you don't know how much time is left,"** says the biochemist. In Switzerland, about one in 3000 people are affected - worldwide, there are 1.5 million. It starts with tunnel vision, then followed by loss of contrast and color, and usually ends with complete blindness. The light-sensitive cells, the photoreceptors, slowly die.

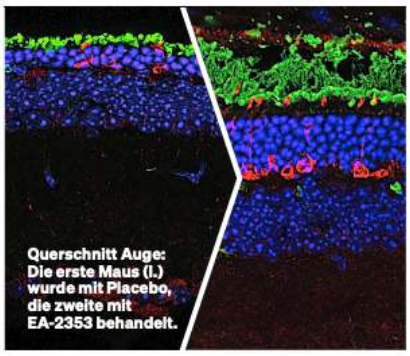
Working with the body, not against it: Matthias Steger, founder of Endogena Therapeutics, researches endogenous regenerative medicines.

What if the destroyed photoreceptors in the retina could be regenerated? Like the lizard's tail that has fallen off and grows back on its own? This is exactly what Endogena Therapeutics, based in Schlieren ZH, is working on. The premises with offices and laboratory are furnished with a lot of light, color and design - on a poster you can see in 2000-fold magnification what

Steger and his team are working on: he activated cones and rods in the cross-section of the eye of a previously blind mouse.

In these laboratories in the Bio- Techno-Park in Schlieren ZH, research is being conducted into new therapies against blindness.

The image documents a scientific sensation, at least in a mammal. "To date, no one has shown that photoreceptors can be regenerated in the adult eye," Steger said. **This kind of regeneration often happens in our bodies all by itself, without us paying much attention to these processes.** When old cells die, new cells grow back - in organs such as the heart and liver or in tissues such as skin, cartilage or muscle. Skin cells renew themselves completely within a month. Other cells do so only slightly or not at all, as in the eye: **"If the photoreceptors of the retina are damaged, they cannot renew themselves."**



Cross-section eye: The first mouse (l.) was treated with placebo, the second with EA-2353.

Even in his early career at Hoffmann-La Roche more than 20 years ago, Steger was involved in the design and synthesis of active molecules for a variety of therapeutic indications. At the pharmaceutical multinational, the biochemist has had a stellar career, most recently as Head of Global Research and Technology Partnerships. For Steger, who gets up at 5 am, goes jogging and dashes to work on his racing bike, the traditional pharmaceutical industry was no longer agile enough at some point: "I saw the opportunities that lie in this novel method against degenerative diseases. With my own company, I can be more dynamic."

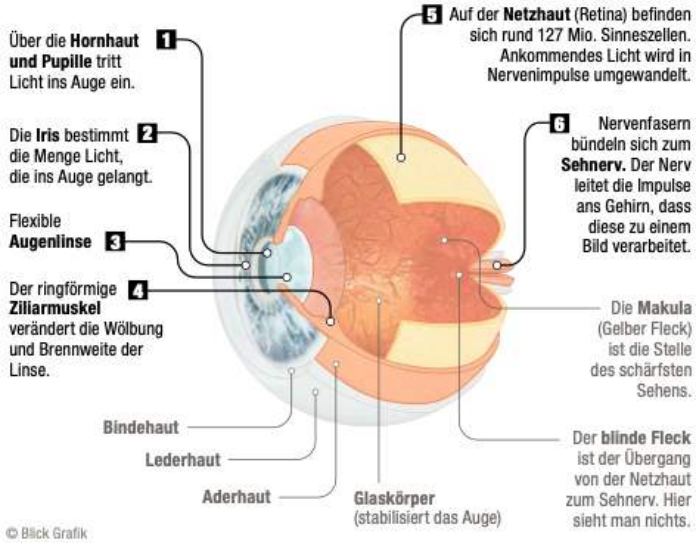
The idea behind the drug treatment called EA-2353: **retinal stem cells are "awakened" from their dormant state with the appropriate molecules**. Over the years, the researcher has created his own chemical library of 2000 molecules for Endogena Therapeutics: "They're the most important currency in our industry; big pharmaceutical companies have over a million test chemicals." Molecules are like keys that open the lock to the biological pathway and thus

regulate it. Finding the right one to develop an effective therapeutic is detective work. "It's like the famous search for a needle in a haystack. It's possible thanks to artificial intelligence and faster data analysis," says the researcher. Only after several thousand tests does a signal show up, a so-called “hit”.

In this way, Endogena Therapeutics has identified around 20 active molecules, developed them further and, in a first step, tested them i*n vitro*. "We have shown in the test tube that we can activate retinal stem cells," says Steger. This approach was successfully tested in blind mice. Steger: "Various tests show that the mice were able to see again!"

The human eye

Vision functions as an interaction of cornea, iris, lens and sensory cells.
But it is the brain that "translates" the incoming nerve impulses into an image.



1. Light enters the eye through the **cornea** and **pupil**
2. The **iris** controls the amount of light that enters the eye
3. Flexible **lens**
4. The annular **ciliary muscle** changes the curvature and focal length of the lens
5. 127 million sensory cells are located on the **retina** - incoming light is converted into nerve impulses
6. Nerve fibers bundle to form the **optic nerve**. The nerve transmits the impulses to the brain, which processes them into an image.

Makula - The **macula** (yellow spot) is the site of sharpest vision.
Blinde Fleck - The **blind spot** is the transition from the retina to the optic nerve. Here you see nothing.

Glaskörper - vitreous body (stabilizes the eye)
Aderhaut - choroid
Lederhaut - sclera
Bindehaut - conjunctiva

The clinical trial in 14 blind patients will be completed next summer. It will be at least another three years - if all goes well - before EA-2353 is launched on the market. Because the method does not reverse the genetic defect, the chemical, which is injected into the eye, must be re-

administered regularly. Hope is high, he says: "We receive up to 20 inquiries a day from those affected," says Steger.

Endogena Therapeutics is not the only biotech company conducting research in the fight for eyesight. Other clinical trials in retinitis pigmentosa are also currently underway. One person keeping tabs on research efforts in the field is Christian Grimm, 60. The professor, Head of Research at the Eye Clinic at the University of Zurich, says: "Most of them are working with gene and stem cell therapies and optogenetics." The latter is based on the finding that even bacteria and algae can perceive light with specialized proteins. **A virus serves as a "taxi" thus delivering the genetic blueprint for light-sensitive proteins to diseased retinal cells.** In one case study, this enabled a previously blind patient to recognize objects again, but he also needed specially designed glasses to do so. "For someone who is blind, even small steps mean improvement," Grimm said.

Science has not yet achieved the biblical miracle of the blind man seeing again. "Right now, there are many approaches. Of those, a lot won't work, but among them will be a method that makes a breakthrough," Grimm says. Teams in many labs are researching using the body's own stem cells, which are then returned to the eye as reprogrammed cells. But that's a complex process, he says: "The cells first have to be taken from the patient, then reprogrammed and differentiated. All this under absolutely sterile conditions," Grimm explains. For Grimm, Endogena's approach has a decisive advantage: **"The application by means of an injection is simple and non-invasive."** However, Grimm warns against premature euphoria, also in the interest of those affected.

Could the method help the children from Canada keep their eyesight? As a scientist, Matthias Steger does not want to make any predictions before he can provide proof: "The treatment is actually most successful in young patients, before the degeneration of the eye and retina sets in." If the method works, it could lead the way for the treatment of other degenerative diseases such as dementia, muscle weakness or osteoporosis. At Endogena Therapeutics, the next clinical trial is already underway, on the most common cause of blindness after the age of 50: age-related macular degeneration, or AMD for short. Steger: "Modern medicine has solved many problems, so we are getting older. But not the infirmities that come with it." Endogenous regenerative medicine is a new approach: "Here we work with the body, not against it."

Endogenous regenerative medicine

The basis for the Endogena Therapeutics method is the discovery by the Japanese scientist Shinya Yamanaka, who in 2006 showed how he could specifically activate dormant genes in body cells. **Through this specific reprogramming, body cells could be restored to their embryonic state.** Inspired by his collaboration with Yamanaka, Matthias Steger founded Endogena Therapeutics in 2016, a biopharmaceutical company that aims to harness the potential of endogenous stem cells (endogenous = "originating inside the body") to treat diseases.