



Pitt develops 'living eye drop' for healing eye damage



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When Anthony St. Leger abandoned a petri dish for a week in his lab in 2017, he didn't expect it to change the trajectory of his work.

"My whole career is based on a mistake," he joked.

The professor of ophthalmology and immunology at the UPMC Vision Institute had discovered a bacterium, *C. mastitidis*, growing in the dish. Since then, the lab has been working to genetically engineer it, to learn more about its relationship to the eye surface and discover how it might be harnessed to treat eye diseases and infections.

[Millions of U.S. adults](#) have dry eye disease, and [hundreds of thousands scratch their corneas every year](#), making corneal abrasions the most common kind of eye injury.

A key protective layer for the eye, the cornea is one of the quickest-healing parts of the body. But these chronic diseases, as well as inflammation of the cornea and viruses such as herpes and shingles that can infect the eye, have few treatments besides regular application of eye drops.

And [a 2011 study](#) found most people don't adhere to an eye drop schedule, especially when prescribed to apply the drops multiple times a day. Young men in the study were most likely to not adhere. [A 2022 study](#) also found that just 10% of people adhered to their eye drop regimen. Researchers in Portland, Ore., even [developed a dropper with an alarm](#) in its cap that measures compliance and beeps on a schedule.

St. Leger's lab genetically engineered the living bacteria to secrete a protein called IL-10, which regulates immune responses in the body. Whereas bacteria in the gut, say, need to die before they release a therapeutic, St. Leger and his team were able to target specific sequences in the code of the *C. mastitidis* to get it to release IL-10 while still living.

Mice with eye abrasions who were given the IL-10 solution healed quicker than mice in the control group, which only got a saline solution. To confirm the IL-10 was helping to heal the mice's wounds and not another immune pathway, they administered an IL-10 blocker and saw the advantages disappear.

"The fact that it worked was kind of surprising," said St. Leger. "We haven't seen any sort of negative effects" of the engineered bacteria yet.

Researchers hope the finding can lead to a product that can heal eye conditions in people — using a bacterial strain that already colonizes the eye's surface — though that possibility is years away. [Results of the study were published](#) March 5 in Cell Reports.

On a top floor of the UPMC Mercy Pavilion in Uptown, Jackie Shane transferred a yellowish liquid into vials that sat in a pink lattice. Swimming inside was that bacteria, which Shane would later splice and modify for different purposes: Some help the bacteria anchor to the cell surface, and others might produce substances that aid in nerve growth.

Shane, a postdoctoral researcher in St. Leger's lab and lead author on the paper, spent many months handling mice, ticking a light scratch onto their corneas and dropping the lab's "living eye drop" into their eyes to observe

healing. The lab also created a version of the eye drop modified from human genes to ensure it was compatible with human cells.

Deval Paranjpe, chair of ophthalmology at Allegheny Health Network, was excited by the study's findings and the potential of the novel eye drop.

"No one has ever really done this before that's been so widely reported," she said. "In the future, this might be a good way of delivering needed healing factors to the eye."

Paranjpe noted the modularity of the eye drop was especially exciting for creating future technologies — that is, the same format might be used elsewhere on the body if researchers swap out different genes, she said.

It's not new that bacteria can be genetically modified to express certain proteins or act as a drug delivery vehicle. In 2006, 10 patients with Crohn's disease took capsules with modified bacteria. That bacteria, like St. Leger's, expressed the protein IL-10. After one week, most patients reported relief from symptoms, and markers of inflammation had decreased.

St. Leger and his team want to keep tinkering with their technology and develop a kind of "off-switch" once the bacteria has done its job, to prevent overcolonization, bacterial resistance or unknown negative effects of applying a living bacteria onto the eye surface.

"One of the biggest concerns about something like this is you want to have as much control as possible," he said. "We have this bacterium that stays on the eye for an indefinite period of time. At that point, you lose control of [it]. If you want to take it away, or if you want to stop producing that factor, we don't have that control quite yet."

Studying the ocular microbiome, too, is nascent and has ample room for growth and innovation. While trillions of bacteria colonize our gut, for instance, one bacteria for every 50 cells lives on the eye.

"We are looking forward to being able to make this more targeted toward diseases that afflict a broad range of people," he said.

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