

RESTORING VISION IN PEOPLE WITH BLINDING DISEASES

In December 2017 the U.S. Food and Drug Administration (FDA) announced [approval](#) of a novel gene therapy, Luxturna, to treat patients with a rare form of inherited vision loss. It is the first gene therapy approved in the United States to target a disease caused by mutations in a specific gene. In this case, the RPE65 gene, which affects vision. For [Dr. Jean Bennett](#), the physician scientist behind this medical breakthrough, being able to change the prognosis for people who are blind or losing their vision — and to see the profound impact that this has on their life — has been a career well spent.

Luxturna works by delivering a normal copy of the RPE65 gene directly to retinal cells. These retinal cells then produce the normal protein that converts light to an electrical signal in the retina to restore a patient's vision loss. Luxturna uses a naturally occurring adeno-associated virus, which has been modified using recombinant DNA techniques, as a vehicle to deliver the normal human RPE65 gene to the retinal cells to restore vision.

Dr. Bennett, the F.M. Kirby Professor of Ophthalmology at the University of Pennsylvania, describes the factors that enable this particular gene therapy to work as a perfect storm: “We’ve got this Trojan horse (the recombinant virus) essentially delivering the normal copy of the DNA that is missing in the target cells; we’ve got tissue (the retina) that does not reject foreign antigens; and we have a tightly enclosed space (the eye) where we can deliver these new genes very, very efficiently and under direct visualization to the target cells. And then we can monitor the function of those cells without causing any discomfort or pain to the patient.”

However, just like a perfect storm involves a rare combination of circumstances, the basic science that led to this treatment for blinding diseases required the convergence of decades of work by Dr. Bennett, a massive international effort to map the human genome, and enormous advances in biomedicine. All of which, involved the National Institutes of Health.



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During a post-doctoral fellowship Dr. Bennett worked with a researcher at NIH who was seeing children in his lab with various genetic disorders and her interest in developing gene therapies really took off. However, getting from point A to point B required learning more about these diseases and going to medical school. It was at Harvard Medical School that she met her husband and their focus on the retina took root: his studies in neuroscience morphed into studies of the retina and she gained further expertise in genetic engineering and genetics. While they discussed gene therapy for the eye back then, no one knew — in the 1980s — which genes caused retinal diseases.

But then came the 1990s and the [Human Genome Project](#). While Dr. Bennett was focused on developing the methods to manipulate genes and deliver them safely and with good duration — the tools needed for gene therapy — the Human Genome Project was enabling the identification of genes, that when mutated, caused different genetic diseases, including the RPE65 gene and its role in blindness.

It still took another 20 years to fully deliver on her goal: a gene therapy to treat blindness. And along the way the NIH was a constant presence. Dr. Bennett credits the NIH for not only supporting her work, but for shaping her career.



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