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A Stem-Cell Therapy for Blindness

Advanced Cell Technology will seek approval for human trials of its treatment for vision loss

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An experimental therapy using human embryonic stem cells to treat degenerative eye diseases has proved safe and effective in animal studies, and may begin early human trials in the next few months if it receives approval from the Food and Drug Administration. If granted approval, the therapy will be the second embryonic-stem-cell-based treatment to progress to human trials, and it will provide a test case for further applications of stem cells.

While scientists have made huge advances using stem cells to treat diseases in animal models, testing these experimental therapies in humans poses some unique challenges. One is proving that the cells are safe: embryonic stem cells, which can develop into any tissue type in the body, carry the risk of forming tumors. Another challenge is the threat of immune rejection of the transplanted cells; in most cases, introducing foreign cells would require a patient to take powerful drugs for life to suppress the immune system, as is the case with organ transplants. For that reason, the first stem-cell therapies have focused on the eye and nervous system, so-called immune-privileged sites that do not experience this response to foreign cells. [Geron](#), a biotech company based in Menlo Park, CA, received FDA approval in January for a trial to treat patients with acute spinal-cord injuries with cells derived from embryonic stem cells.

This latest treatment for eye disease, developed by [Advanced Cell Technology](#) (ACT), based in Worcester, MA, uses human embryonic stem cells to re-create a type of cell in the retina that supports the photoreceptors needed for vision. These cells, called retinal pigment epithelium (RPE), are often the first to die off in age-related macular degeneration and other eye diseases, which in turn leads to loss of vision. Several years ago, scientists found that human embryonic stem cells could be a source of RPE cells, and subsequent studies found that these cells could restore vision in mouse models of macular degeneration.

In a recent study published online in the journal [Stem Cells](#), researchers from ACT and Oregon Health Sciences University show that their stem-cell therapy provides a long-term benefit in animal models of vision loss. A second experiment tested the long-term safety of the cells in mice--an important requirement for moving into human testing--and found no evidence that the cells cause tumors.

To test the efficacy of the cell transplants, the researchers injected RPE cells derived from embryonic-stem-cell lines into the eyes of rats with a genetic defect in their RPE that causes their vision to gradually deteriorate. After three months, the retinas of treated rats had many more photoreceptors than those of

untreated diseased rats, and the treated animals performed better in vision tests; however, their performance in the tests diminished with time. The transplants were also able to improve vision in a mouse model of Stargardt's disease, a rare but untreatable illness that causes blindness early in life.

Robert Lanza, chief scientific officer at ACT, says that the study is an important step toward bringing the therapy into clinical trials, as it includes more detailed safety studies and uses cells produced under the strict manufacturing conditions that are required for human applications. To ensure the quality and consistency of cell therapies, the FDA has laid out extensive guidelines for preparing cells and testing them for any potential disease-causing pathogens. Lanza says that after completing this and two other animal studies under the guidelines, the company will be set to file an application with the FDA to begin clinical trials in the coming months.

Lanza believes that the RPE treatment is a promising early application for embryonic-stem-cell therapies. Not only does it avoid the problem of immune rejection, but the cells themselves are relatively easy to create, as embryonic cells tend to spontaneously differentiate into RPE cells and can be easily maintained in that state. "This is absolutely one of the perfect first therapies," Lanza says. ACT will focus first on patients with Stargardt's disease, which is an "orphan" disease--a rare disease with no available treatment that qualifies for federal tax incentives for clinical trials. Lanza believes that the therapy is likely to work well because the supporting tissue that RPE cells must attach to is still intact in these patients. The next patient population would be those with age-related macular degeneration, a much more common disease in which gradual deterioration of tissue in the retina leads to vision loss.

[Thomas Reh](#), a neurobiologist at the University of Washington who is unaffiliated with ACT, agrees that the RPE therapy is a promising candidate for translating embryonic-stem-cell therapies to the clinic. However, he cautions that the *Stem Cells* study does not provide the "slam dunk" that he had expected to see. Although the transplants did restore visual function in the eye, the benefit was not always sustained over time in animals.

Reh says that these experimental therapies rely on the assumption that cells generated from embryonic stem cells will function like their normal counterparts. But the less-than-stellar results suggest that the cells may not represent an exact replacement, he says. Scientists won't know for sure until they see how the cells perform in clinical trials.