Stem-Cell Aid May Soon Treat Some Blindness

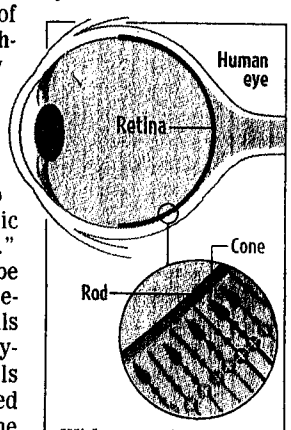
By Sharon Begley

AMID THE POLITICAL debate over whether and when embryonic stem cells might prove medically useful, scientists today are announcing a laboratory advance they say could soon lead to human tests of a stem-cell treatment for two common forms of blindness.

In a paper to be published in the fall issue of the journal Cloning and Stem Cells, and posted on that journal's Web site today, scientists describe experiments in which they grew human embryonic stem cells and induced them to develop into specialized cells of the human eye. The research involved both stem cells approved for research by President Bush as well as some from a private lab that are off-limits to federally funded researchers.

The specialized eye cells, called retinal pigment epithelium cells, are crucial for vision because they provide nutrients to and eliminate waste from the rods and cones—the eye's light receptors. When the RPE cells deteriorate, so do the rods and cones, leading to diseases such as age-related macular degeneration, a progressive disease that is the leading cause of blindness in people over 50. There is no good treatment for the disease, which afflicts an estimated nine million Americans.

"Retinal-cell transplants could be one of the first applications of human embryonic stem-cell technology," says one of the study's leaders Robert Lanza, medical director of **Advanced Cell Technology**, a closely held biotechnology company in Worcester, Mass. "With the right resources, we hope to get this into the clinic in one to two years."



Without retinal pigment epithelium cells, the eye's **rods and cones** *can deteriorate, causing blindness.*

That goal may be overly optimistic, because the retinal cells grown from embryonic stem cells haven't been tested on animals, let alone on people, to determine if they are both safe and effective in restoring vision. Such tests could take five years.

Advanced Cell has scored several notable firsts—its scientists were the first to clone an endangered species, the cow-like gaur, which died soon after birth. It has also been aggressive in trumpeting its achievements. In 2001, for instance, the company reported it had cloned a human embryo, but the embryo failed to develop beyond the six-cell stage. Advanced Cell is currently seeking to raise money through a private placement.

Scientists who weren't involved in the retinal-cell study, but who have reviewed it, were nevertheless impressed. "This is a very important step," says Sally Temple of Albany (N.Y.) Medical College, a leading expert in neuronal stem cells

...lers resolution of 1980 x 1080—the numi... is pretty exciting," he says.

Stem Cells Offer New Hope for Blind

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It had been thought that scientists would have to manipulate stem sells in some way to get them to develop into a desired cell type, such as by growing them in a mixture of nutrients containing some sort of differentiation-inducing molecules. But Dr. Lanza and Advanced Cell's Irina Klimanskaya found that the stem cells didn't need any help. While growing in a lab dish, they spontaneously differentiated—first into neurons and then into the retinal cells.

To the scientists' surprise, the cells were not only indistinguishable from adult retinal cells, but resembled these cells more closely than do existing lines of such cells.

The retinal cells derived from embryonic stem cells could become a source of replacement cells for people losing their vision to age-related macular degeneration or retinitis pigmentosa, which affects an estimated 200,000 Americans, says Albany Medical College's Prof. Temple.

Transplants to restore vision in animals have been promising. In March, scientists at Kyoto University Hospital in Japan reported that they had induced embryonic stem cells from monkeys to turn into retinal pigment epithelial cells. When they transplanted those cells into rats with retinal damage, they allowed the retina's rods and cones to thrive.

Retinal-cell transplants in people, however, have produced mixed results. "RPE-cell transplants, some using cells from cadavers and some from fetuses, have not been successful in most of the patients," says Marco A. Zarbin, professor and chair of the Institute of Ophthalmology and Visual Science at the University of Medicine and Dentistry of New Jersey, in Newark. In a few cases the patient's immune system seemed to reject the transplant, while in others the layer of tissue that the retinal cells must attach to in order to function was abnormal, due either to disease or to age.

Transplanted fetal retinal cells seem to stick to that surface, even when it is old or diseased, better than transplanted adult retinal cells do, which raises the hope that retinal cells from embryonic stem cells will too. In a 1999 study, for instance, 14 patients with retinitis pigmentosa received fetal retinal transplants. There was no rejection of the transplant for the 44 months the patients were studied. In five of the patients vision improved.

And last month physicians in Kentucky reported that they had transplanted a sheet of fetal RPE and related cells into one eye of a patient with retinitis pigmentosa. Her vision improved enough to read large-print magazines.

"There is no sign of rejection and the improvement is real," says Norman Radtke of Norton Audubon Hospital, Louisville, who performed that surgery. Dr. Radtke warns, however, that RPE cells alone mightn't be sufficient to restore vision; related retinal cells might also be required.

The Advanced Cell team found that all embryonic stem-cell "lines," or colonies of stem cells being kept alive in a nutrient medium in a lab dish, aren't alike. For their experiment, the scientists obtained 11 such lines. Three were created in 1998 and approved for research by President Bush in August 2001; 22 such lines are now available, says the National Institutes of Health. Any stem cells created after that date are off-limits to federally funded studies.

The Advanced Cell scientists also used six embryonic stem-cell lines created using private funding by Douglas Melton of Harvard University, Cambridge, Mass.. Finally, Dr. Lanza's team created stem-cells lines from two blastocysts—days-old balls of cells—donated by couples who had completed fertility treatment and had no plans to have the embryos implanted in the woman's uterus.

The White House-approved stem cells didn't differentiate well, Dr. Lanza says: "We wouldn't have made this discovery if we had been limited to the stem-cell lines approved by the president."

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