Stem cells improve visual function in blind mice

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Central vision is lost in age-related macular degeneration after cells in the retina deteriorate. New research by Stephen Tsang suggests special adult stem cells could restore sight or prevent vision loss.

An experimental treatment for blindness, developed from a patient's skin cells, improved the vision of blind mice in a study conducted by Columbia ophthalmologists and stem cell researchers.

The findings suggest that induced pluripotent stem (iPS) cells – which are derived from adult human skin cells but have embryonic properties – could soon be used to restore vision in people with macular degeneration and other diseases that affect the eye's retina.

"With eye diseases, I think we're getting close to a scenario where a patient's own skin cells are used to replace retina cells destroyed by disease or degeneration," says the study's principal investigator, Stephen Tsang, MD, PhD, associate professor of ophthalmology and pathology & cell biology. "It's often said that iPS transplantation will be important in the practice of medicine in some distant future, but our paper suggests the future is almost here."

The advent of human iPS cells in 2007 was greeted with excitement from scientists who hailed the development as a way to avoid the ethical complications of embryonic stem cells and create patient-specific stem cells. Like embryonic stem cells, iPS cells can develop into any type of cell. Thousands of different iPS cell lines from patients and healthy donors have been created in the last few years, but they are almost always used in research or drug screening.

No iPS cells have been transplanted into people, but many ophthalmologists say the eye is the ideal testing ground for iPS therapies.

"The eye is a transparent and accessible part of the central nervous system, and that's a big advantage. We can put cells into the eye and monitor them every day with routine non-invasive clinical exams," Tsang says. "And in the event of serious complications, removing the eye is not a life-threatening event."

In Tsang's new preclinical iPS study, human iPS cells – derived from the skin cells of a 53-year-old donor—were first transformed with a cocktail of growth factors into cells in the retina that lie underneath the eye's light-sensing cells.

The primary job of the retina cells is to nourish the light-sensing cells and protect the fragile cells from excess light, heat, and cellular debris. If the retina cells die – which happens in macular degeneration and retinitis pigmentosa – the photoreceptor cells degenerate and the patient loses vision. Macular degeneration is a leading cause of vision loss in the elderly, and it is estimated that 30 percent of people will have some form of macular degeneration by age 75. Macular degeneration currently affects 7 million Americans and its incidence is expected to double by 2020.

In their study, the researchers injected the iPS-derived retina cells into the right eyes of 34 mice that had a genetic mutation that caused their retina cells to degenerate.

In many animals, the human cells assimilated into mouse retina without disruption and functioned as normal retina cells well into the animals' old age. Control mice that got injections of saline or inactive cells showed no improvement in retina tests.

"Our findings provide the first evidence of life-long neuronal recovery in a preclinical model of retinal degeneration, using stem cell transplant, with vision improvement persisting through the lifespan," Tsang says. "And importantly, we saw no tumors in any of the mice, which should allay one of the biggest fears people have about stem cell transplants: that they will generate tumors."

Tsang hopes to begin a clinical trial for macular degeneration patients in the next three years, after more preclinical testing in animal models.

Already a similar trial – testing retina cells derived from embryonic stem cells – has seen encouraging preliminary results. A paper from this study, published earlier this year, reported that the stem cells are safe and have potential to improve the vision of two patients with macular degeneration.

"These results are encouraging, but iPS cells could be a more attractive option than embryonic stem cells," Tsang says, "because patients may not need drugs to prevent rejection of the transplanted cells."

Regardless of which cell works better, the prospect of stem cell transplants may mean many people with macular degeneration may never lose their vision.

"We have a good idea which patients will eventually lose their vision. In the early stages of macular degeneration we can tell by looking in the eye, and new genetic tests can now predict vision loss with 70 percent accuracy even before those signs emerge," Tsang says. "If the therapy is safe, we could intervene very early to prevent much vision loss."

The study was published online in advance of print in the journal *Molecular Medicine*.

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