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## Cell transplants now potential treatment for retinal degeneration

For two decades, scientists have studied how to transplant cells into the eye to correct a variety of visual disorders. The acid test for such an

approach is whether cell transplants can actually maintain spatial vision. New joint American and Canadian research in this field provides encouraging results suggesting that transplanting cells into the retina can significantly limit the deterioration of spatial vision in rats.

Blindness can occur when photoreceptor cells in the retinal cell layer or retinal pigment epithelium cells in the adjacent layer of cells deteriorate. The retinal pigment epithelium (RPE) layer, under normal conditions, provides a supportive housekeeping role to the rod and cone photoreceptor cells. If the RPE does not function correctly, the environment for the rods and cones can deteriorate rapidly.

One approach to counter such deterioration would be to provide a fresh supply of either healthy RPE cells or other types of healthy cells that could provide the same functions as RPE cells. Many research groups worldwide have conducted such tests and have shown considerable photoreceptor protection, sustained visual threshold responses, and improved behavioural responses using cell transplantation.

The newest research, from the Department of Psychology and Neuroscience in the Canadian Centre for Behavioural Neuroscience at the University of Lethbridge, and from the Moran Eye Centre at the University of Utah, now demonstrate that such cell transplantation treatments can have a significant impact on visual acuity. The research team published their findings in the journal *Vision Research* this summer.

The research group used Royal College of Surgeon (RCS) rats as their model of retinal degeneration. In these rats, the degeneration results from a mutation in a gene known as "Mertk." Mertk is expressed in the RPE where it encodes a tyrosine receptor kinase protein believed to be involved in the recognition and binding of outer segment debris produced as a by-

product of photoreceptor cell activity. The defect in Mertk compromises the ability of the RPE to dispose of the outer segment debris from photoreceptor cells; the resulting accumulation of debris leads to photoreceptor degeneration and blindness.

The group's data have shown that delivery of human RPE cells and human Schwann cells into the retina of the rats can preserve spatial vision, in some cases up to 70% of normal. The study provides further support that cell transplantation may become a viable treatment for retinal degenerative disease.

The researchers used two different cell types for transplantation – human RPE cells and human Schwann cells. Schwann cells

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were used in the study because they are known to produce many of the growth factors that provide a healthy environment for the photoreceptor neuronal cells. The researchers grew the two cell types in the lab in culture dishes before concentrating them into a small volume of liquid to deliver to the rats' eyes.

Using a fine glass pipette attached by tubing to a Hamilton syringe, the cell suspensions were delivered to the sub-retinal space through a small scleral incision. Either 200,000 RPE cells or 20,000 Schwann cells were delivered in 2 microlitres of fluid to the retina of the rats.

The visual acuity of the animals was tested using a visual perception task known as the Visual Water Task. The apparatus to record such data consists of a trapezoidal-shaped pool with a mid-line divider extending into the pool to create a Y-shaped maze with a stem and two arms. Two computer monitors face into the wide end of the pool; the animals are trained to discriminate between different visual stimuli projected on the computer screens. The rats readily learn to swim towards the platform

that allows escape from the water.

After transplantation with the human RPE cells, the rats were tested from four to seven months of age; the results demonstrated that transplanted animals had a higher acuity than control animals at all ages. The visual acuity of animals receiving Schwann cell transplants were tested at four and five months of age and also showed that the acuity of the transplanted animals was significantly better than the controls.

The researchers concluded that the use of either immortalized human RPE cells or freshly harvested Schwann cells were capable of providing a significant benefit to vision in an animal model.

The report claims to be the first to present a systematic quantitative study examining spatial vision thresholds in animals following sub-retinal cell transplantation.

Using either of the cell types carries both advantages and disadvantages. The human RPE cells have the obvious advantage of replacing into the retina the same cell type that normally resides in this tissue under normal conditions. However, the source of such cells will likely require a parallel use of immuno-suppressants to insure that the transplanted RPE cells are not attacked and destroyed by the body's immune system. Also, because RPE cells are derived from a laboratory immortalized cell line, there is the risk that such cells may replicate in an uncontrolled manner, leading to an additional pathology.

On the other hand, Schwann cells would carry no such replication risks. Schwann cells may be harvested from another part of the patient's body, such as a peripheral nerve. Because such cells come from the same patient, no immunosuppressant drugs would be required.

From their findings, the researchers com-

mented that because Schwann cells "have benefit to vision not very different from the RPE cells in an animal model of retinal degenerative disease, it is clear that with the potential of performing autologous transplantation, the path from laboratory investigation is significantly simplified with this cell type."

Although using Schwann cells in such a treatment approach does not address the primary defect of the Mertk gene, the approach does clearly extend the length of useful vision. In the absence of a "cure," extending such useful vision in a human patient would represent a significant "second best" and, as such, represents a most welcome advance.

## Glossary

**Retinal pigment epithelium:** refers to a pigment cell layer situated behind the photoreceptors that nourishes the retinal cells. The retinal pigment epithelium is attached to the choroid, a layer filled with blood vessels that nourish the retina.

**Royal College of Surgeon (RCS) rats:** are a widely used animal model of inherited retinal degeneration.

**Mertk:** Mertk is a protein expressed in the RPE where it is believed to be involved in the recognition and binding of outer segment debris produced as a by-product of photoreceptor cell activity. Mutations in Mertk disrupt the ability of the RPE to phagocytose debris from photoreceptor cells resulting in accumulation of unwanted material eventually leading to cell degeneration and blindness

**Tyrosine receptor kinase protein:** proteins that play an important role in mediating cell signalling processes.

**Schwann cells:** A type of cell of the peripheral nervous system that helps separate and insulate nerve cells.

**Visual Water Task:** a specialised training task used to assess behavioural response in rodents under specific experimental conditions.