New research using neural progenitor cells derived from human fetal stem cells may offer a novel method for preserving vision in degenerative disease, for which there is no effective treatment.

Stem cell therapy shows promise for rescuing deteriorating vision

A new study in rats has used neural progenitor cells, formative brain cells that arise in early development, derived from human fetal stem cells in an attempt to restore vision. The cells show some of the best rescue, functionally and anatomically, from degenerative eye disorders in animals whose eyesight was likely to be lost from degenerative disease.

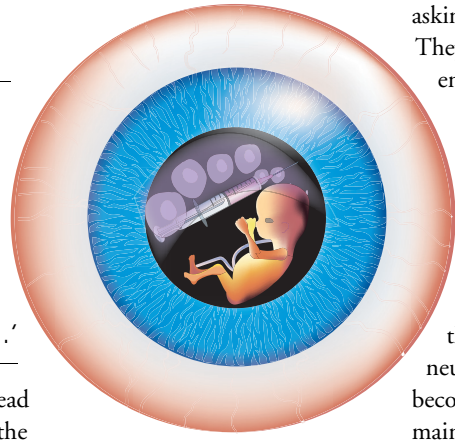
'Macular degeneration is the leading cause of registered blindness for people over the age of 50 years in the western world…'

David Gamm, the lead author of the study at the University of Wisconsin-Madison (WI, USA), explained that the animal models of disease showed close similarities to human eyes and the degenerative diseases that afflict humans.

Macular degeneration is the leading cause of registered blindness for people over the age of 50 years in the western world and, currently, there are no effective methods for preserving eyesight in patients suffering from degenerative eye disease.

The stem cells were being examined for their ability to deliver a specific growth factor in models of Parkinson's disease and Lou Gehrig's disease, but it was uncovered that the cells alone actually appeared to show an ability to rescue vision.

The new findings appear in the journal *Public Library of Science One* and suggest that there may be novel ways to preserve vision. The results came as a surprise according to Raymond Lund, an author of the study and an eye disease expert at the University of Utah (UT, USA).



The cells were being used to move glial cell line-derived neurotrophic factor (GDNF) into the eyes as a continuous delivery system, in order to be able to avoid repeated injections to the eyes. Lund commented that, "The idea was to use the cells as a continuous delivery system, but we found they work quite well on their own."

Lund explained, "On their own, they were able to support retinal cells and keep them alive".

He continued "We didn't expect that at all. We've used a number of different cell types from different sources and these have given us the best results we've ever got."

David Gamm explained the novel use of progenitor cells, "This cell type isn't derived from the retina. It is derived from the brain," he explained, "but we're not asking it to become a retina. They survive in the environment of the eye and don't disrupt the local architecture. They seem to live in a symbiotic relationship." He concluded, "It seems that the cells in and of themselves are quite neuroprotective. They don't become retinal cells. They maintain their own identity, but they migrate within the outer and inner retina."

The authors agree that further research is required to understand how the cells work to protect against degeneration. "The first thing is to show that something works, which we have done," explained Lund. "Now we need to find out why, but this is a good jumping off point."

Source: Gamm DM, Wang S, Lu B *et al.*: Protection of visual functions by human neural progenitors in a rat model of retinal disease. *PLoS ONE* 2(3), e338 (2007).

Type 2 diabetes is linked to increased risk for Parkinson's disease

Individuals with Type 2 diabetes are at an increased risk for Parkinson's disease (PD), according to a new study.

Scientists from the National Public Health Institute (Helsinki, Finland) have organized the largest prospective study to date, examining the prevalence of Type 2 diabetes among patients with PD. The study concluded that Type 2 diabetes is a risk factor for PD patients, with an 83% increased risk compared with the general population.

"Although the association between Type 2 diabetes and PD is not as great as that of coronary heart disease or stroke, this finding is still clinically important and something clinicians should pay attention to," explained Gang Hu, lead author of the study.

The prospective, population-based study involved 51,552 Finnish men and women for a mean follow-up period of 18 years. No participants had a history of PD but 633 patients developed the disease during the trial. It was found that patients with diabetes were significantly more likely to develop the disease.

"It could be hypothesized that diabetes might increase the risk of PD partly through excess body weight," explained Hu. The mechanism behind this association between diabetes and Parkinson's disease is not known but these findings call for further research.

Source: Hu G, Pekka J, Bedel S: Type 2 diabetes and the risk of Parkinson's disease. *Diabetes Care* 30, 842–847 (2007).

in brief...

A randomized, double-blind, placebo-controlled study of venlafaxine XR in out-patients with tension-type headache.
Zissis N, Harmoussi S, Vlaikidis N *et al.*: *Cephalalgia* 27(4), 315–324 (2007).
This randomized, double-blind, placebo-controlled study aimed to evaluate the safety and efficacy of venlafaxine extended release (XR) in the prophylactic treatment of out-patients with tension-type headache (TTH). Patients were treated with 150 mg/day venlafaxine XR or placebo for 12 weeks. The results indicated a decline in the number of days patients experienced headaches, achieving a significantly greater decrease compared with placebo, thus providing preliminary evidence for the efficacy and safety of XR venlafaxine 150 mg/day in reducing the number of days with TTH.

Potential for treatment of liposarcomas with the MDM2 antagonist Nutlin-3A.
Muller CR, Paulsen EB, Noordhuis P *et al.*: *Int. J. Cancer* (2007) [Epub ahead of print].
This study investigated the molecular response to The MDM2 antagonist Nutlin 3A treatment in several liposarcoma cell lines. Nutlin efficiently stabilized p53 and induced p53-dependent downstream transcription and apoptosis in liposarcoma cells lines in the presence of amplified MDM2 *in vitro*. Nutlin was also effective on cell lines without amplified MDM2 but with wt tp53, stabilizing p53 but not inducing apoptosis. Nutlin represents a promising new therapeutic principle for the treatment of an increasing group of sarcomas.

Olanzapine-induced weight gain in anorexia nervosa: involvement of leptin and ghrelin secretion?
Brambilla F, Monteleone P, Maj M. *Psychoneuroendocrinology* (2007) [Epub ahead of print].
A 3-month course of olanzapine (OLA) 2.5 mg for 1 month and 5 mg for 2 months was administered to ten patients suffering from anorexia nervosa, ten patients received placebo. Cognitive behavioral psychotherapy and programmed nutritional rehabilitation was used to back-up OLA treatment. The aim of the study was to determine if modulation of regulatory peptides leptin and ghrelin were responsible for weight gain in patients with anorexia nervosa, previously reported in other studies. Body mass index increase was observed but did not differ significantly between OLA and the placebo group. No correlation with leptin and ghrelin was seen, concluding that weight gain observed in OLA-treated patients was not linked to drug administration.

Nonsurgical treatment for epilepsy and Parkinson's disease

A new technique has been designed that is able to reversibly silence brain cells. Scientists from the MIT Media Lab (MA, USA) used pulses of yellow light to inhibit the activity of specific neurons.

Scientists hope that this new technique could be used in the treatment of epilepsy and Parkinson's disease (PD), in which neurons misfire causing some of the pathological features of the diseases. It is thought that the silencing of haywire neuron activity could be controlled by optical brain prosthetics, eliminating the need for irreversible brain surgery.

Edward Boyden, leader of the MIT Media Labs Neuromedia Group explained, "In the future, controlling the activity patterns of neurons may enable very specific treatments for neurological and psychiatric diseases, with few or no side effects."

The laser pulse targets the *halorhodopsin* gene found in bacteria. Neurons can be engineered to express the *halorhodopsin* gene and pulses of yellow light are able to inhibit neuron activity. Light activates chloride pumps, enabling chloride ion movement into neurons, causing the voltage to be lowered, thus silences them.

The technique offers an insight into which brain regions and neurons contribute to specific behaviors or pathological states in certain diseases.

Source: Han X, Boyden ES: Multiple-color optical activation, silencing, and desynchronization of neural activity, with single-spike temporal resolution. *PLoSONE*. MIT media lab http://pubs.media.mit.edu

Mild IVF treatment could help reduce the burden of multiple births

A study of 404 patients undergoing *in vitro* fertilization (IVF) has indicated that mild ovarian stimulation with one transferred embryo can be successful in producing similar rates of live term babies when standard stimulation is used on two transferred embryos.

Ester Heijnen, lead author of the study, explained that, "We aimed to test the hypothesis that mild IVF treatment can achieve the same chance of a pregnancy resulting in term live birth within 1 year compared with standard treatment, and can also reduce patients' discomfort, multiple pregnancies, and costs."

A randomized, noninferiority effectiveness trial conducted at the University Medical Centre in Utrecht, The Netherlands, used gonadotropin-releasing hormone (GnRH) antagonist combined with single embryo transfer or stimulation with a GnRH and transfer of two embryos, which is the standard treatment.

The percentage of live births after 1 year was 43.4% for couples using mild treatment with one embryo transfer and 44.7% with the standard treatment involving two embryos. The results also demonstrated that 13.1% of couples experienced multiple births when using the standard treatment compared with 0.4% using the mild treatment.

Heijnen speculated, "Mild IVF treatment might lessen both patients' discomfort and multiple births, with their associated risks".

Source: Eijkemans MJ, De Klerk C, Polinder S *et al.:* A mild treatment strategy for *in-vitro* fertilization: a randomized non-inferiority trial. *Lancet* 369(9563), 743–749 (2007).

Progression of atherosclerosis stopped by high-dose Lipitor®

New trials led by doctors from the Academic Medical Center in Amsterdam have offered patients with familial hypercholesterolemia (FH) hope for the treatment of atherosclerosis. Research by Pfizer has successfully proven that the progression of atherosclerosis can be halted by high doses of their statin Lipitor® by employing the use of two new imaging techniques.

The head-to-head trials investigated the efficacy of toretrapib in combination with Lipitor, versus Lipitor as a monotherapy. Results were presented at the American College of Cardiology in March.

Lipitor doses of 23 and 56 mg were administered to the trial subjects and indicated halting of the progression of atherosclerosis. Lipitor resulted in plaque regression in the most diseased part of the coronary artery. In a second arm of the trial, lower doses of Lipitor were seen to allow atherosclerosis progression.

Many drugs are studied in head-to-head trials with imaging techniques but Lipitor is the first statin to have been investigated in this way. Over 2800 patients were involved in three studies to investigate toretrapib versus Lipitor and Lipitor alone, using intravascular ultrasound (IVUS) and carotid B-Mode ultrasound (CBUS).

IVUS is a 3D imaging technique used to measure the total plaque volume over the length of the vessel. Carotid ultrasound, also used in the study, measures the thickness between the inner and middle layers of the carotid artery wall allowing accurate data of atherosclerosis progression to be obtained.

"From a clinical perspective, what is remarkable in these studies is that Lipitor was able to stop the progression of disease, including the most difficult to treat FH patients studied" explained John Kastelein, lead investigator for the trials.

Kastelein commented that, "These results support previous studies where higher doses of Lipitor have demonstrated an impact on atherosclerosis. However, while imaging findings are scientifically interesting, we know that physicians make clinical decisions based on proven cardiovascular outcomes."

Source: Kastelein JJP1, van Leuven SI1, Evans G *et al.*: Designs of RADIANCE 1 and 2: carotid ultrasound studies comparing the effects of torcetrapib/atorvastatin with atorvastatin alone on atherosclerosis. *Curr. Med. Res. Opin.* 23(4), 885–894 (2007).

New HPV vaccine filed for US FDA approval

The experimental human papillomavirus (HPV) vaccine, Cervarix™, has been filled for US FDA approval. The drug is 100% effective against infection with HPV strains 16 and 18, which are responsible for over 70% of cervical cancers, Cervarix also protects against the strains 31 and 45. The FDA-approved drug Gardasil®, is already offered to women and girls aged 9–26 years, and advised to be given to girls aged 11 to 12 years. Gardasil protects against HPV strains 6 and 11, vulval cancers and two HPV-linked cancers. FDA approval for Cervarix is expected between October and January 2008.

Source: GlaxoSmithKline www.gsk.com/media/pressreleases.htm [Press release].

Rabies-based vaccine could be effective against HIV

Researchers have used the rabies virus to deliver HIV-related proteins into animal subjects. Results show that 2 years after initial vaccination, four primates were protected from disease even after exposure to virulent animal–human viruses.

Matthias Schnell, Professor of microbiology and immunology at the Thomas Jefferson University (PA, USA), constructed the rabies vector that contained one of two different viral proteins, a glycoprotein present on the surface of the HIV virus or an internal protein from simian immunodeficiency virus (SIV).

The research involved immunizing four primates with both vaccines, while two animals received only a weakened rabies virus. After the first injection, booster shots were given, but no enhanced immune response was seen. A new vector was developed containing a viral surface protein from the vesicular stomatitis virus (VSV) and administered. 2 years after the initial administration, booster vaccines were given containing the rabies-VSV vector and specific immune responses were observed.

The animals that had been administered the preliminary vaccine managed to control the infection, whereas the control animals experienced high levels of the virus present in the blood and a decrease in $CD4^+$ T cells, with one control macaque dying of an AIDS-like disease.

Schnell explained, "We still need a vaccine that protects from HIV infection, but protecting against developing disease can be a very important step."

This research underlines that the technique is possible but the vaccine construction is a long way from being used in humans to protect from HIV. Future larger studies on primates are currently underway.

Source: McKenna PM, Koser ML, Carlson KR *et al.*: Highly attenuated rabies virus-based vaccine vectors expressing simian-human Immunodeficiency virus89.6P env and simian immunodeficiency virusmac239 gag are safe in rhesus macaques and protect from an AIDS-like disease. *J. Infect. Dis.* 195(7), 980–988 (2007).