MedicalXpress

First report of long-term safety of human embryonic stem cells to treat human disease

October 15 2014

New research published in *The Lancet* provides the first evidence of the medium-term to long-term safety and tolerability of transplanting human embryonic stem cells (hESCs) in humans.

hESC transplants used to treat severe vision loss in 18 patients with different forms of macular degeneration appeared safe up to 3 years post-transplant, and the technology restored some sight in more than half of the patients.

"Embryonic stem cells have the potential to become any cell type in the body, but transplantation has been complicated by problems including the risk of teratoma formation and immune rejection", explains lead author Professor Robert Lanza, Chief Scientific officer at Advanced Cell Technology in the USA. "As a result, immunoprivileged sites (that do not produce a strong immune response) such as the eye have become the first parts of the human body to benefit from this technology."

In the two phase 1/2 studies, hESCs were differentiated into retinal pigment epithelium cells and transplanted into nine patients with Stargardt's macular dystrophy and nine patients with dry atrophic age-related macular degeneration, the leading causes of juvenile and adult blindness in the developed world, respectively. No effective treatments exist for either condition, and eventually the light-receiving (photoreceptor) cells of the retina degenerate leading to complete blindness.

All participants were injected with one of three different doses of retinal cells (50 000, 100 000, and 150 000 cells) into the subretinal space (under the retina) of the eye with the worse vision.

The hESC-derived cells were well tolerated for up to 37 months after transplantation. No safety concerns (eg, hyperproliferation or rejection) in the treated eyes were detected during a median follow-up of 22 months. Adverse events were associated with vitreoretinal surgery and immunosuppression, but none were deemed to be related to the hESC-derived cells.

Follow-up testing showed that 10 out of 18 treated eyes had substantial improvements in how well they could see, with 8 patients reading over 15 additional letters in the first year after transplant. Visual acuity remained the same or improved in seven patients, but decreased by more than 10 letters in one patient. Importantly, untreated eyes did not show similar visual improvements.

According to co-lead author Professor Steven Schwartz from the Jules Stein Eye Institute, Los Angeles, USA, "Our results suggest the safety and promise of hESCs to alter progressive vision loss in people with degenerative diseases and mark an exciting step towards using hESC-derived stem cells as a safe source of cells for the treatment of various medical disorders requiring tissue repair or replacement."[2]

Writing in a linked Comment, Anthony Atala, Director of the Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Winston-Salem, NC, USA says, "The work by Schwartz and colleagues is a major accomplishment, but the path to get to this point has not been smooth. Since the discovery of hESC in 1998, much has transpired, including political, ethical, and scientific debates, with an overall push to achieve the promise of human therapies. Now, we have follow-up that extends to longer than 3 years in patients treated with

hESC-derived stem cells, showing both safety and apparent efficacy...Much work remains to be done before hESC and induced pluripotent stem cell therapies go beyond regulatory trials, but the path is now set in motion.

Provided by Lancet