EXTRACT FROM MACULAR DISEASE FOUNDATION AUSTRALIA RESEARCH UPDATE 2015 ~ 4 December 2015

Stem cell treatment

The Foundation respects different points of view concerning stem cell research. The Foundation's role is simply to report on key research for your information.

Stem cells are special types of cells that have the remarkable ability to change into other cell types. The new "differentiated" cells can be grown in the laboratory and then be transplanted into organs such as the eye to replace damaged or dead cells.

Sources of stem cells:

Human embryonic stem cells (hESCs)

One or two cells are removed from an embryo produced from *in vitro* fertilisation. These cells are then cultured in the laboratory and can produce a virtually endless supply of stem cells which can be coaxed into becoming the desired cell type. hESCs are the most adaptable type of stem cell as they can be converted into almost any type of cell.

Adult stem cells

These are usually obtained from either umbilical cord blood, or from bone marrow. These cells are more limited in the types of other cells they can produce.

Induced pluripotent stem cells (iPSC)

Certain types of adult cells such as skin or retinal cells can be re-programmed to revert back to being a type of stem cell, although they are more limited as to the type of new cell that can be formed.

In the healthy eye, RPE cells lie under the photoreceptor cells, providing them with nutrition and removing waste products. In AMD, RPE cells become unhealthy or die which then leads to the loss of central photoreceptor cells and hence central vision loss. Initially, most stem cell research has been directed to the use of stem cells to produce new RPE cells which can then be implanted into the eye.

The first human studies in this area are primarily to confirm the safety of implanted RPE cells. Initial studies are in a small number of people with very poor vision.

The ultimate aim of RPE cell replacement is for the procedure to be performed in people with earlier stage disease, so that the new RPE cells can prolong the function of existing photoreceptors. For people who have already lost significant vision, it is likely that their photoreceptors will have already died, and therefore, implantation of both RPE and photoreceptor cells may be needed. The development of photoreceptors from stem cells is much more complex and their success will depend on the new photoreceptors being able to make viable connections with the nerves leading to the brain. This is much more challenging.

Several human trials using stem cells for AMD have now started in other countries, although none have started yet in Australia.

Ocata Therapeutics (previously Advanced Cell Technology)
In June 2015, the American company Ocata reported follow-up results from four phase 1 trials on the use of hESC-derived RPE cells in people with very poor vision from late stage dry AMD (geographic atrophy) or Stargardt's disease. 31 patients were included in these trials with some having four years of follow-up. None of the 31 patients experienced any safety issues relating to uncontrolled growth of the implanted cells, rejection or serious side effects. Almost all of the patients experienced improved or stable vision, although specific details were not announced. As a result of these initial results, Ocata has now enrolled their first patients into a phase 2 trial in people with late stage dry AMD and Stargardt's disease. Another trial in people with myopic macular degeneration is also due to start.

London Project to Cure Blindness After ten years of laboratory work and planning, this group reported in September 2015 that the first patient with sudden vision loss from wet AMD had received RPE cells derived from hESCs, implanted as a sheet under the retina. The project is being coordinated by Moorfields Eye Hospital in London, one of the world's leading clinical research institutions in eye diseases. Ten patients will be enrolled initially and followed for 12 months to assess safety and stability of these cells.

Riken, Japan
In September 2014, doctors in Japan performed the first transplant of retinal tissue derived from "induced pluripotent stem cells". These are stem cells that can be created from a person's own tissue and therefore provide a perfect genetic match, meaning the new cells should not be

rejected by the body's immune system. There should also be no need for anti-rejection drugs. In May 2015, Riken announced that they had successfully produced a three dimensional structure in a culture dish containing multiple layers of retinal cells, including rod and cone photoreceptors. They have also shown that the edge of the structure can grow, suggesting that when implanted into the eye, the photoreceptors may be able to connect with the existing nerve tissue, which is critical if these cells are to ultimately restore sight.

The future for stem cell treatment
Many other stem cell projects are now underway at other centres. Human trials have not yet commenced in Australia.

Several more years work is required before any stem cell treatment is expected to gain registration and become readily available.

Please Note: There are currently no registered (approved) stem cell derived treatments for AMD available anywhere in the world.
Despite this, there are companies selling expensive, unproven and unregistered "treatments" for AMD using products that are claimed to be stem cells. Promotion of these 'treatments' typically involves dubious testimonials but little or no real evidence of safety or efficacy in AMD. Some of these treatments may be dangerous. The Foundation strongly advises all patients to talk with their eye specialist before committing to any unusual treatment.

Macular degeneration in the media
There are regular reports in the media about important research breakthroughs in the field, however many of these reports can be inaccurate or misleading. The Foundation constantly reviews the global media and endeavours to provide factual, objective and current information on latest developments.

If you need further information on a media story, please see the Foundation's website or call on 1800 111 709.