Macular Disease Foundation Australia
Extract - Research Update - December 2016

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.

To give an indication of the scale of the research effort in this field, there are now over 40 institutions and companies that are working with stem cell treatments for AMD and other eye diseases.

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 move back to a type of stem cell, although they are more limited as to the type of new cell that can be formed.

Replacing cells

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.

To date, the greatest progress has been made with embryonic stem cells as these are the most adaptable form of stem cell. One company (Ocata) has now been implanting RPE cells derived from embryonic stem cells into people with very poor vision from dry AMD or Stargardt's disease for several years, with no apparent safety issues, and in some people, vision appears to have improved.

Another well-publicised study at the University College in London recently started the use of stem cell derived RPE in people with wet AMD.

Embryonic stem cells however pose ethical issues for some people, so significant effort is being made to 'turn back' certain adult cells (such as skin cells) into stem cells, which can then be reprogrammed into the desired cell such as RPE cells.

To avoid the risk of rejection when cells from one person (the donor) are implanted into another person (the patient or recipient), Japanese researchers at the Riken Institute have successfully taken a patient's

own skin cells and converted them to stem cells, which have then been coaxed into retinal cells. These cells have then been implanted into the same person, taking the place of the damaged cells. Unfortunately, this process is very slow and prohibitively expensive.

In 2016, the same researchers are looking at ways to make the technology practical and affordable. They have created banks of stem cells created from skin cells from many donor adults. They then analyse certain proteins called MHCs on the surface of the cells, which play a key role in the immune response. By matching the MHCs of the donor cells with the MHCs of the patient, they appear to able to avoid rejection issues and may remove the need for life-long anti-rejection drugs.

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. However, to model and better understand the disease process, research in Melbourne is using human stem cell derived retinal tissue. This is important as we do not have a good animal model of the disease process. 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.

Products that have not been successful

Drug development is an expensive, high risk process, and large numbers of treatments fail to demonstrate sufficient efficacy or safety to be registered. During 2016, several potential treatments that have been reported in this summary in previous years have failed to meet

expectations and are not being pursued. These include: Emixustat, Isonep, LFG316, Eculizumab, Isonep, Pazopanib, NT-503.

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.

Macular Disease Foundation Australia - Research Grants Program

The Foundation's Research Grants Program is a major contributor to Australian research into macular degeneration. To date almost $3 million has been committed to leading Australian researchers to undertake exciting and critical research. A new round of grants will be opened in April 2017.

If you would like to donate to the Macular Disease Foundation Australia Research Grants Program call 1800 111 709 or donate online at www.mdfoundation.com.au

Please note: Research is a lengthy, expensive, high risk process. Many of the projects in this summary are still many years from completion and some will not make it through the rigorous development and clinical testing process. The Foundation has prepared this summary based on information available at the time of publication, and it is not intended to describe all aspects of the relevant research. Circumstances are also likely to change. The Foundation does not accept liability for out of date, misinterpreted or incorrect information. This summary does not constitute advice and you should discuss treatment options with your doctor. Discussion of a project does not constitute the Foundation's endorsement of that product or treatment, and should not be used for investment or treatment decisions. The Foundation is unable to recommend or facilitate the entry of any clients into a particular clinical trial as all trials have strict inclusion and exclusion criteria.

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