Stem cell therapy

There are no stem cell treatments currently available commercially for people with an inherited retinal disease (IRD).

There are clinical trials of stem cells for some forms of IRD, but none of these trials are presently in Australia.

If you would like to find stem cell projects that are open to participants, please refer to the Retina Australia Research Project and Clinical Trial Register. To find out whether stem cell therapy is an appropriate option for you or your family member, please speak to your ophthalmologist.

What is a stem cell?

A stem cell is an unspecialised cell with the unique ability to develop into specialised cell types in the body.[1] They can divide indefinitely to produce new cells.

In addition, in many tissues they serve as a sort of internal repair system, dividing to replenish other cells.

- In the eye, an example is the limbal stem cells of the cornea (front transparent tissue of the eye). Due to the exposed nature of the cornea, the cells need to be replaced regularly. This is achieved through replication of the limbal stem cells.
- Unfortunately, the retina does not have stem cells in place, and so cannot repair itself.

When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialised function, such as a muscle cell, a red blood cell, or a brain cell.

Types of stem cells

There are three types of stem cells:

1. Adult stem cells

- Adult stem cells are an undifferentiated cell found within a tissue or organ.
- Adult stem cells in mature tissues have a currently unknown origin.[1]
- They supply new cells as an organism grows and replace the damaged cells of the tissue in which they are found.
- Adult stem cells are multipotent, meaning they can only change into certain cell types (i.e., epithelial stem cells can only provide cells that make skin and hair).

2. Embryonic stem cells – ESCs

- ESCs supply cells for an embryo as it grows, and are pluripotent, meaning they can change into any cell type.[1]
- Human embryonic stem cells (hESCs) are derived from a preimplantation embryo produced by in vitro fertilisation and donated for research purposes with informed consent of the donors.

3. Induce pluripotent stem cells – iPSCs

- iPSCs are made in the laboratory by taking normal cells (i.e., skin cells) and reprogramming them to become stem cells that can develop into any cell type (i.e., they are pluripotent).[1]
- They can divide indefinitely to produce new cells.
- To generate iPSCs, signals are introduced to switch off any genes that tell the cell to be specialised, and switch on genes that tell the cell to be a stem cell.

Cell therapy research for inherited retinal disease

For the purposes of investigating disease mechanisms, and for developing treatments for IRDs, pluripotent stem cells (hESCs and iPSCs) have been successfully differentiated into both retinal pigment epithelium (RPE) cells and photoreceptors. However, only stem cell-derived RPE cells have currently been investigated in clinical trials.

Stem cells for developing treatments for IRDs

Previous trials have used stem cells to grow these RPE cells, which can then be implanted into the eye to replace dead cells in a diseased retina.

- This has been done in people with age-related macular degeneration, Stargardt disease and retinitis pigmentosa.
- Trials have investigated several delivery methods, including injecting the cells in a suspension, and placing them on a "scaffold" which is then implanted as a layer underneath the retina.
- As of December 2023, there have been no regulatory-approved stem cell treatments for IRD.

Stem cells for patient-derived models for pre-clinical research

In addition to developing stem cells as a treatment, many research teams are using stem cells as patient-derived laboratory models for preclinical research.

- In these studies, samples of blood, skin or hair are taken from people with an IRD. Scientists are then able to turn these patient samples into iPSCs, which can be grown in the laboratory.

- The cells grown will have the same genetic mutation as the patient who donated the sample, and so can be used to learn more about the specific mutation, investigate how the cells function when they have the mutation, or to screen new drugs and potential treatments for that specific IRD.

Stem cell therapy projects supported by Retina Australia

Retina Australia has supported some stem cell therapy projects through its annual grant program in recent years. These include:

- 2024: Characterising Stargardt Disease Mutations for Splice Intervention Therapeutics, Dr Di Huang – Lions Eye Institute, Perth, $60,000
- 2023: Establishing novel AAV gene editing for Usher Syndrome, Dr Anai Gonzalez-Cordero – Children's Medical Research Institute, Sydney $55,774
- 2020: Single cell RNA sequencing to characterise cell diversity and molecular signatures of hiPSC-derived retinal organoids, Dr Anai Gonzalez-Cordero – Children's Medical Research Institute, Sydney $39,490
- 2020: Development of regenerative therapy for retinitis pigmentosa using cellular reprogramming, Raymond Wong – Centre for Eye Research Australia, University of Melbourne. $40,00
- 2018: Utilising patient-specific retinal organoids in vitro to investigate the effects of an SNRNP200 mutation causing early onset Retinitis Pigmentosa, Dr Carla Mellough – Lions Eye Institute, Perth. $40,000
- 2018: Microglia and retinal degenerations: Identifying key modulators of inflammation as therapeutic targets, Associate Professor Riccardo Natoli – Australian National University, Canberra $39,951
- 2017: Large scale generation of retinal pigment epithelium cells from patient induced pluripotent stem cells, Associate Professor Alice Pebay – Centre for Eye Research Australia, Melbourne. $40,000
- 2016: Cone photoreceptor development and cell death mechanisms, Dr Livia S Carvalho – Lions Eye Institute/University of Western Australia, Perth $40,000
- 2014: Accelerating therapeutic discoveries for retinitis pigmentosa, Professor David Mackey AO – Lions Eye Institute, Perth $140,000
- 2013: The role of gliosis in advanced retinal degeneration, Associate Professor Erica Fletcher – University of Melbourne $40,000

References
(1)National Institutes of Health. Stem Cell Information: https://stemcells.nih.gov/. Accessed 22 February 2020/

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