Autumn 2015 : Edition 10

Macular*NEWS*

Welcome to the 10th edition of Macular*News*.

In this issue we tell you about our plans to use stem cells grown from patients with macular disease in an effort to learn about what is causing the disease.

We also hope to turn these stem cells into the various cells that we believe cause macular disease and use them as a treatment.

This is a long-term goal with many challenges but we believe that we should be working at the cutting edge of science, which these cells certainly are.

Prof. Mark Gillies
Macular Research Group

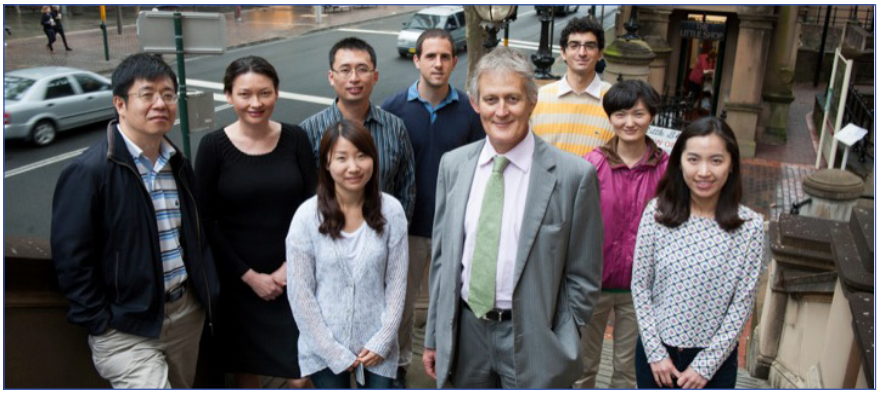
Diary Date:
Friday 23 October 2015
9.30am - 12 midday
Macular Information and Research Update
To register call (02) 9382 7316 or visit https://maculardegeneration2015.eventbrite.com.au

Macula Research Laboratory Scientists

The Laboratory Research Unit of the Macula Research Group conducts applied research that is ultimately designed to identify better treatments for macular disease.

In previous issues we have described a particular mouse model they produced which develops many of the features that cause loss of vision in most retinal diseases: leakage from retinal blood vessels, growth of abnormal retinal blood vessels and degeneration and loss of the “photoreceptors”, which are the cells that pick up light.

Professor Mark Gillies directs the team, which is led from day to day by Dr Weiyong Shen, an ophthalmologist from China who also has an extensive record of laboratory research, particularly in gene therapy and modelling retinal disease in animals. Ling Zhu is a senior “postdoc” who has experience gained in the US in molecular biological techniques. Sook Chung, a junior postdoc who is highly proficient technically, is conducting the stem cell work described in this issue.



The Macular Research Group Laboratory Science Team Back (L to R): Dr. Weiyong Shen, Dr. Svetlana Cherepanoff, Dr. Ling Zhu, Dr. Brian Lyons, Dr. Nathan Coorey and Dr. Ying Wang. Front (L to R): Ms So-Ra Lee. Prof. Mark Gillies, and Dr. Sook Hyun Chung.

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Are stem cells the future for treating macular degeneration?

Stem cells are undifferentiated biological cells that can grow indefinitely with an ability to turn into any type of cells in the body (this ability is called pluripotency).

Stem cell research, especially human embryonic stem cell research, holds great potential to treat many diseases such as cancer and diseases in central and peripheral nerve system. However, there are considerable ethical concerns around the use of human embryos.

In 2006, Prof. Shinya Yamanaka at Kyoto University in Japan, found a way to make induced pluripotent stem cells (iPS cells) by reprogramming the skin cells of adult mice with specific genomic factors (so called Yamanaka factors: OCT4, SOX2, KLF4, and c-MYC).

Shortly after the successful animal experiments, he successfully made human iPS cells from human adult skin cells and won a Nobel Prize in 2012 as a result.

iPS cells began a new era of stem cell research because they have many of the characteristics of embryonic stem cells whilst avoiding ethical concerns as the cells come from the patient.

This also means that they will not be rejected if they are grafted back for example as nerve cells into the brain or the retina.

In the future, iPS cells may be used to treat diseases in a variety of ways. They may be

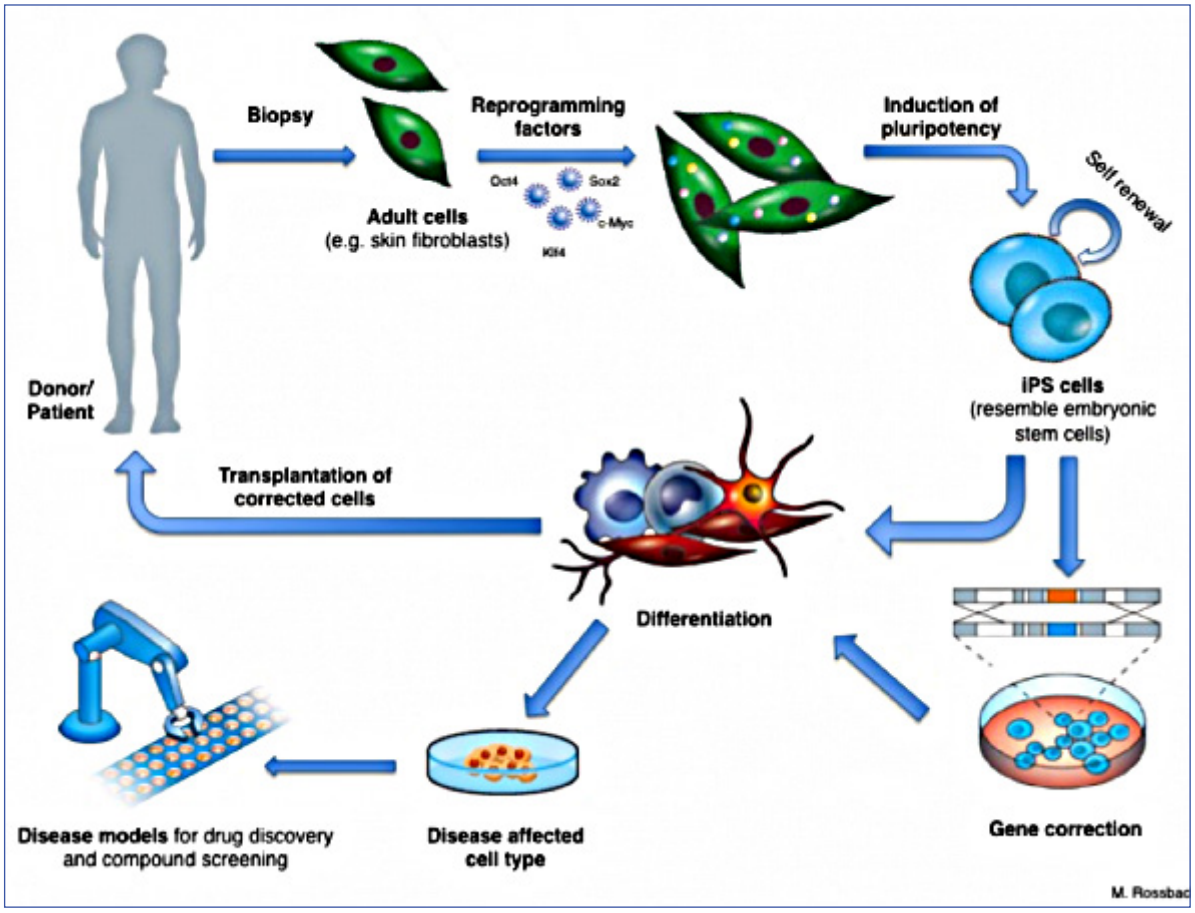

Figure 1: shows how induced pluripotent cells are made from a patient's skin biopsy and what they can be used for. Cells taken from the skin biopsy are grown in a dish. They are then turned into stem cells using "reprogramming factors", which is a major scientific advance. If the cells are taken from patients with a disease caused by a single gene defect, this can be corrected and the cells can theoretically be put back into the body to replace the diseased cells. This is already starting for some diseases, but most macular diseases cannot yet be treated in this way because they are caused by a combination of many gene defects which are not yet completely understood. The other use is that the cells presumably have the same defect as the patient, because that is where they came from. So they can be studied in a dish and tested in various ways to find out what is causing the disease. This is what we are trying to do for macular disease. We also intend to develop the cells into the various cell types that make up the retina and put them back in the patient's retina, but that is a long-term vision.*

used to replace cells that have worn out.

Readers of this newsletter are likely to be aware that transplanting photoreceptors is something we hope to do in future, although we will also need to transplant retinal pigment epithelial cells to support the photoreceptors.

It's a bit tricky and we are certainly still several years away from clinical use.

Another potential clinical use of iPS cells is to replace genetically defective cells with freshly made cells where the genetic defect has been repaired.

The other use of iPS cells are to model disease in a dish in order to understand the disease better and potentially find new treatments, which is what we are doing.

One recent report that has moved the field forward more quickly than expected is that iPS cells can be induced by applying the right factors at the right time to actually assemble retinas in a dish.

Use of iPS cells in Macular Telangiectasia Type 2

We are using this cutting edge iPS cell technology in our laboratory to investigate potential causes and future treatments for macular degeneration. As we have

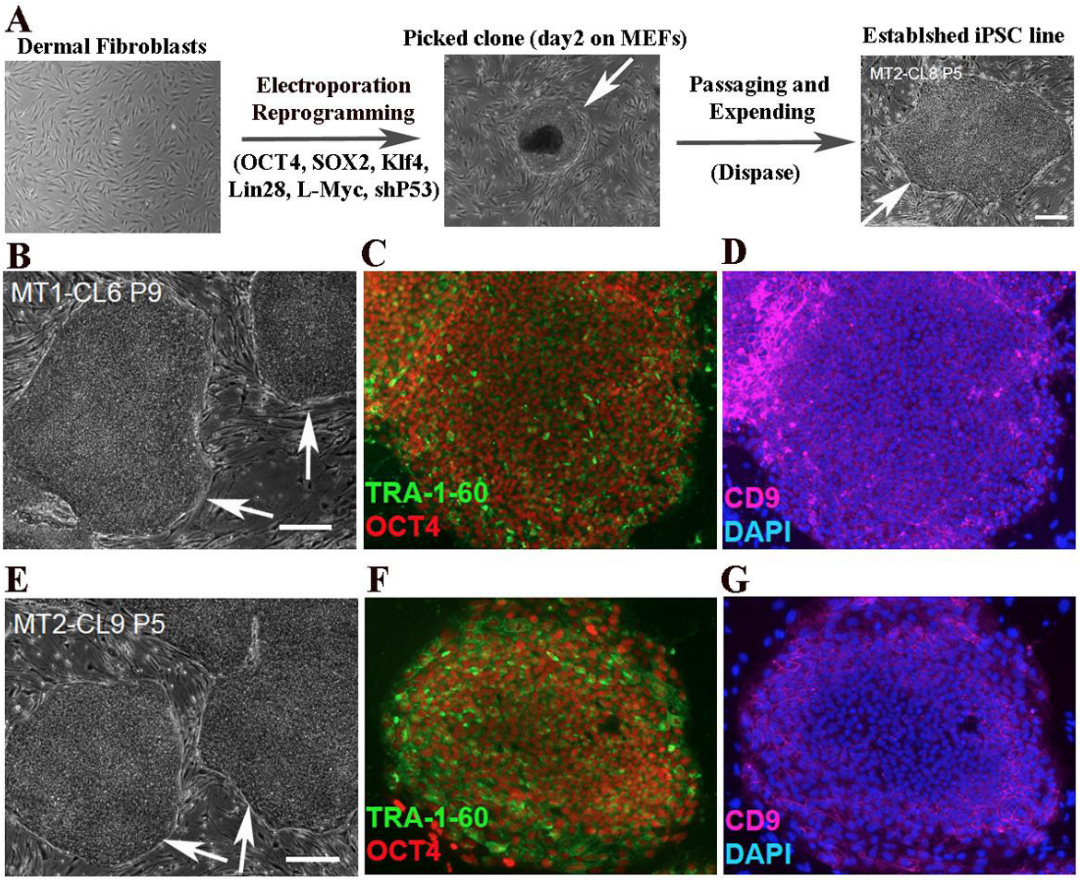

Figure 2: shows the progress we have made so far in making these iPS stem cells. (A) shows the cells grown from the skin biopsy of a patient with macular disease. They were reprogrammed to produce stem cells, which can be seen as little islands, each of which has grown from a single stem cell (B). These "clones" are grown up to produce a cell "line" which has come from a single stem cell (C). The middle row shows cells from one of our patients "stained" with coloured antibodies that detect the stem cell markers shown, demonstrating that they really are stem cells. In the third row are 2 stem cell clones from a second patient with macular disease that are positive for the same stem cell markers.

written in previous editions of Macular*News*, we believe that a deficiency of Muller cells, the major supporting cells nurturing other neurons, may contribute to macular degeneration.

If we can identify what this is we might find a better treatment.

In our laboratory, we are currently using iPS cells from patient skin biopsy samples to model macular degeneration in a dish.

We have obtained patient skin biopsy samples from Prof. Mark Gillies clinic and successfully reprogrammed them into iPS cells with Yamanaka factors in collaboration with an internationally recognised stem cell research group, Dr. Alice Pebay's laboratory, at the Centre for Eye Research Australia in Melbourne.

Our goal is to differentiate patient derived iPS cells into retinal cups in the laboratory and isolate Muller cells from the retinal cups.

After this, we will study the Muller cells to understand what is wrong with them and how it might be fixed.

**iPS cells derivation and its applications (http://www.eurostemcell.org/factsheet/ips-cells-and-reprogramming-turn-any-cell-body-stem-cell)*

Contact Us

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We thank and acknowledge our loyal supporters, without whom this important research could not take place.

Save Sight Institute is a centre of The University of Sydney.

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If you would like to make a tax-deductible donation or a bequest to support macular research please contact us:

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