



# I-C

## Newsletter of Retina Australia (ACT) Inc

EDITION 2-2012

June 2012

### MESSAGE FROM THE PRESIDENT

Welcome to the second newsletter for 2012, with which comes details of what promises to be an extremely worthwhile 2012 Retina Australia Congress, being hosted by RA (NSW). The title of the Congress, *Hope In Sight*, is a reflection of the optimism held by both the national and global RP communities that the pace of research into a cure for retinal dystrophies bodes well for all of us. As always, reports of recent research progress are contained within this issue, as is the story of a remarkable fundraising effort.

We would again ask members to take particular note of a request herein regarding participation by ACT members in the Inherited Retinal Diseases Register administered by the Sir Charles Gairdner Hospital in Perth.

Best wishes to all...

**ROBIN POKE**

### MEMBERS' "MONTHLY LUNCH DATE"

Where: Café Charisma  
Shop 4  
2 Colville Street  
North Lyneham

Date: 2<sup>nd</sup> Tuesday of the Month

This is a light and bright café with a delightfully eclectic and very reasonably priced menu, a great ambience and extremely good service. For those who like a drink with lunch, it's BYO.

The next monthly lunch is on:

**Tuesday 10 July 2012**

Please let me know if you have a problem with transport and I will try to arrange for someone to pick you up.

As I am going away for a holiday can you please call Lyn Barlow on **62302 382**

**Jan James**  
**Secretary**  
**Ph 6258 4823**  
**0421 277 880**

## GENERAL NEWS

### SEVEN MARATHONS IN SEVEN DAYS IN SEVEN STATES!!

#### THE 'DIAMOND RUNNER' FINDS A NEW CHALLENGE

In March 2009 Sydney endocrinologist Terry Diamond ran solo from Canberra to Sydney in a bid to improve awareness of osteoporosis and bone disease. *The Diamond Run*, as it was named, was the equivalent of covering a standard marathon (42.125 km) every day for seven days.

Not content with that effort, the seemingly indefatigable Dr Diamond recently found another cause. On Sunday 18 March he began at Uluru a trans-Australia trek that when it ended in Sydney seven days later had seen him run seven marathons in *seven* states!

His new 'cause' was the estimated twenty thousand Australians suffering Retinitis Pigmentosa, the rare, hereditary and currently untreatable eye condition that causes deterioration of the retina and leads to night vision problems, severely limited peripheral vision - and frequently blindness. It is thought many others have milder symptoms.

An Associate Professor of Endocrinology and Metabolic Bone Disease at Sydney's St George Hospital, Terry Diamond incorporated into his seven daily marathons seven Australian icons. His sunrise run at Uluru and his second marathon from Fremantle to Perth were followed by runs over the same distance in South Australia's Barossa Valley, Victoria's Great Ocean Road and Canberra (with the run there ending at Parliament House). Then came a Gold Coast run before the good doctor finally ended his trans-continental odyssey by running from Manly to Sydney's Bondi Beach. Perhaps not surprisingly, Dr Diamond's huge contribution to his cause was badged *The Eye-Con Run*.

"It was a massive undertaking," he said at the end of his journey - "but deliberately so. I wanted to mirror the tough journey and the predicament that sufferers of Retinitis Pigmentosa face every day throughout their lives. Australians are fortunate that the pace of scientific and medical research is rapidly increasing, and that the gift of sight can be restored to many with vision impairments. For sufferers of Retinitis Pigmentosa, however, their loss of sight is presently permanent and untreatable.

"The reality of living with Retinitis Pigmentosa", Dr Diamond added, "is that those suffering the disease must cope with everyday life while seeing their world slowly disappear. Such people face the extraordinary task of living with permanent vision impairment while trying to work towards and succeed at their goals.

"I sought to place Retinitis Pigmentosa in the forefront of public consciousness. I also wanted those presently suffering the disease to know that help in coping with it is available, and that there is hope for their future."

That he succeeded in that task is indisputable.

The President of Retina Australia, Graeme Banks, said his organisation was "immensely grateful" to Dr Diamond.

"It was a supreme effort," he said, having attended the post-finish celebrations at Bondi. "There is little doubt that Terry and his team have made a significant contribution to our overall fundraising target, and we can't thank them enough."

'Team Terry' comprised his great friends Antoinette O'Sullivan and MaryAnne Mason, for whom the logistics inherent in staging *The Eye-Con Run* presented extraordinary challenges.

"The major issue, of course, was the timing involved in such an exercise", said Antoinette.

"Comprising as it did factors such as air travel, car hire, accommodation, meals, laundry - and of course rest! - there wasn't much room for error!

"But we made it, and that's really satisfying."

Antoinette lists as *Eye-Con Run* highlights the Uluru, Ocean Road and Canberra marathons - and of course the finish at Bondi.

"Uluru is sacred to the first Australians so it was both appropriate and symbolic that we started there", she said. "The Great Ocean Road became a 'family affair for Terry when his wife Shani flew down to meet him at the start at Port Lonsdale, then his son, Yoni, ran with him for 15 kilometres to the finish at Bell's Beach. The highlight at Canberra was when newly-appointed Federal Sports Minister, Senator Kate Lundy, came out to meet us at the finish, accompanied by the Parliamentary Secretary for Disabilities and Carers, Senator Jan McLucas. That was a delightful gesture on their part. As for the Bondi finish - say no more! A large media contingent was there and we just had a huge party!"

Proceeds from *The Eye-Con Run* will be used to set up a stem cell research program for sufferers of Retinitis Pigmentosa, in a bid to achieve a therapeutic goal of restoring 20-20 vision in these individuals by... 2020!

At the time of going to press almost \$100, 000 had been raised - but is it enough?

"Not really", the pragmatic Dr Diamond told the media at Bondi. "We need \$100,000 every year for three years."



Terry Diamond surrounded by participants and admirers at the end of the Canberra leg of his Eyecon Run. In the group are RA (ACT) Secretary Jan James, running guru Dick Telford, RA (ACT) president Robin Poke, Terry Diamond, Sports Minister Kate Lundy, Parliamentary Secretary Jan McLucas and members of Dick Telford's running group.

### **NATIONAL CONGRESS**

The 2012 triennial Retina Australia Congress, being hosted this year by Retina Australia (NSW), will be held at The Sebel at Parramatta, west of Sydney, from 19 to 21 October. A special guest is to be Professor Robin Ali from the Moorfields Hospital in London. Professor Ali is a globally recognised expert in stem cell research and gene therapy for those with RP. He is the leader of the group of ophthalmic surgeons who performed the first of the human gene therapy trials at Moorfields.

There will be a host of other interesting speakers on developments in research plus a range of interesting workshops from which to choose. The proceedings will commence on Friday evening with a welcoming Cocktail Party, then on Saturday night there will be a Gala Dinner with professional entertainment and guest speaker Don Burke.

Details of the Congress, including the program and registration details and a range of accommodation and booking information accompany this newsletter, and members are encouraged to attend. Arrangements are being put in place by RA (ACT) for a one-day excursion on the Saturday of the Congress.

## **THE INHERITED RETINAL DISEASES REGISTER**

**In the previous edition of *I-C* we asked that members and their families who had contributed their DNA to the Inherited Retinal Diseases Register being compiled by the Sir Charles Gairdner Hospital in Perth inform the executive of this fact. We pointed out that, within the bounds of personal privacy, it was vital that these statistics be known to us. This is because official figures appear to conflict with what we know from personal enquiries are a conflicting, larger number. There are financial implications inherent in this request. The contribution we in the ACT make to the national 'pot' is contingent on how many members are involved in the program. So again, if this request applies to you (and yours), we would be very grateful if, in the strictest confidence, you would provide our Secretary, Jan James, with this important information.**

## **NEW LUNCH VENUE**

Retina Australia (ACT) has a new venue for its monthly lunches – Café Charisma at North Lynham shops. On 12 June a larger than usual number of members 'sampled' Café Charisma – and declared themselves well satisfied with the choice. The café is light and bright, has an excellent and generously-price menu and the service is excellent. Those who didn't turn up missed a treat and are encouraged to attend the next such event at 12.30 on Tuesday 10 July.

## **RETINA AUSTRALIA YOUTH**

During the past twelve months, a small group of people from across Australia, all of them aged between 18 and 35 and affected by an inherited retinal disease, have combined to establish a Retina Australia Youth Group. Their main aim is to discuss and raise awareness about youth issues relating to their eye conditions and to build a support network. The group has established a "closed group" on Facebook called "Retina Australia – Youths". Anybody who uses Facebook can see the group, and who is in it, but only members see the posts. The Facebook entry states that "this group has been created for those between the ages 18 and 35 who have an inherited retinal disease to network in a comfortable environment and to seek support and information from its members". Two members of the group are planning on attending the youth sessions of the 2012 Retina International Congress in Hamburg in July so that they can network with others of a similar age, learn as much as they can about inherited retinal disease, and share the information and tips from the international group on the Facebook page. If you are in the age group as mentioned, and have an inherited retinal disease, you are encouraged to join the group on Facebook and share your stories. Alternatively, if you know someone who fits these criteria please tell them about the group so that they can join as well. Currently there are nineteen members. We encourage everyone who is eligible to join and assist the Retina Australia youth community to identify key issues and opportunities.

## **SAVE THE DATE! OVERVIEW: 27 AND 28 JULY 2012**

The Canberra Blind Society's free annual assistive technology expo Overview is on again in July and looks to be an exciting one. This year Overview will be themed "Show Me the Way" and will provide the chance to meet assistive technology suppliers and representatives of local low vision and blindness services. Overview is a great opportunity to view the latest developments in a wide range of adaptive technologies, including aids for daily living and print magnification, sophisticated audio and Braille equipment and the latest in computer technology, computer programs and electronic magnifying and closed circuit television

devices. Overview is the only opportunity for people in the Canberra region to view this technology outside the major cities and CBS invites everyone to attend this free event. In addition to the technology display there will also be seminars conducted by local professionals, including Dr Iain Dunlop from the Canberra Eye Hospital and an Orientation and Mobility Instructor from Guide Dogs NSW/ACT. This will provide the opportunity to learn more about eye health and orientation and mobility, and to ask questions of your own. Overview will be held in the Griffin Centre, 20 Genge St Canberra City on Friday and Saturday the 27 and 28 of July. Please call CBS if you have any questions about Overview on, 6247 4580.

## **RESEARCH UPDATE**

### **A REPORT FROM ASSOCIATE PROFESSOR ERICA FLETCHER ON HER RETINA AUSTRALIA AND NH&MRC FUNDED RESEARCH: The role of purines in photoreceptor death during retinal degeneration**

The aim of this project was to examine whether certain substances released from dying photoreceptors could contribute to the death of neighbouring cells. The purine, ATP, is commonly known for its role as an energy molecule. However, when it acts outside cells, it regulates communication between neurons, via receptors called P2X receptors. Our theory was that following neuronal death, large amounts of ATP could be released from dying photoreceptors, which in turn could lead to excessive activation of neighbouring cells and their death.

This project had three aims. First, we examined the mechanism by which ATP induces photoreceptor death. We found that when ATP levels are high, photoreceptor death occurs within 8 hours, via mechanisms involving elevated intracellular calcium and programmed cell death. This work has allowed us to develop a large animal model of retinal degeneration that is currently being used for preclinical testing of the Australian retinal implant produced by Bionic Vision Australia.

Secondly, we examined the effect of inhibition or loss of P2X receptors on retinal structure during degeneration. We have tested a number of compounds known to block the action of P2X receptors. To date, these compounds all reduce photoreceptor death by around 30% in the rd1 mouse model of retinal degeneration. We created and analysed retinal structure and function of P2X7/rd1 double knockout mice and also P2X7null mice. We found that photoreceptor death was slowed in the double knockout also by around 30%, consistent with our pharmacological experiments. We also examined the mechanism by which blockade of P2X receptors reduces photoreceptor death. We expected these experiments to show that photoreceptors die more slowly because they are less activated by the large amounts of ATP. However, to our surprise, we also found that the inflammatory response that normally develops during degeneration was substantially reduced. Thus, the positive effects of drugs that block P2X receptors on photoreceptors could act as anti-inflammatory agents.

The third aim was to establish that anomalies in purine regulation contribute to retinal degeneration. We anticipated that if excessive amounts of ATP contribute to cell death, then one should see evidence that P2X receptors, or the enzymes that degraded ATP are altered prior to or during the active phase of photoreceptor death. We quantified the expression of a range of P2X receptors and also enzymes that degrade eATP in control and rd1 retina. We found that P2X7, P2X4 and NTPDase 1 expression were elevated during the active phase of rod death suggesting that dysregulation of purines occurs during the active phase of degeneration.

In summary, this project has established a possible role for purines in exacerbating photoreceptor death. Moreover, this project has implicated inflammation as a contributor to photoreceptor death. Further work is needed, however, to optimise the use of this class of drug for those with retinal degenerations.

### **EX VIVO GENE THERAPY AND VISION**

Department of Ophthalmology & Visual Science, University of British Columbia, Eye Care Centre, 2550 Willow Street, Vancouver, BC, Canada.V5Z3N9.  
Gregory-Evans K, Bashar AE, Tan M.

Ex vivo gene therapy, a technique where genetic manipulation of cells is undertaken remotely and more safely since it is outside the body, is an emerging therapeutic strategy particularly well suited to targeting a specific organ rather than for treating a whole organism. The eye and visual pathways therefore make an attractive target for this approach. With blindness still so prevalent worldwide, new approaches to treatment would also be widely applicable and a significant advance in improving quality of life. Despite being a relatively new approach, ex vivo gene therapy has already achieved significant advances in the treatment of blindness in pre-clinical trials. In particular, advances are being achieved in corneal disease, glaucoma, retinal degeneration, stroke and multiple sclerosis through genetic re-programming of cells to replace degenerate cells and through more refined neuroprotection, modulation of inflammation and replacement of deficient protein.

### **FIRST PATIENT RECEIVES NOVEL GENE THERAPY FOR CHOROIDERAEMIA**

The first patient to receive gene therapy for an incurable type of blindness was treated towards the end of 2011 as part of a trial led by the University of Oxford. If successful, the advance could lead to the first-ever treatment for Choroideraemia, a progressive form of genetic blindness that first arises in childhood and is estimated to affect over 100,000 people worldwide.

"This disease has been recognised as an incurable form of blindness since it was first described over a hundred years ago", said Professor Robert MacLaren of the University of Oxford, who is leading the trial. "I cannot describe the excitement in thinking that we have designed a genetic treatment that could potentially stop it in its tracks with one single injection."

Jonathan Wyatt, 63, from Bristol, had the surgery at the Oxford Eye Hospital. He is the first of 12 people in this initial human trial to receive the novel gene therapy. Mr Wyatt was diagnosed with choroideraemia in his late teens and has suffered progressive sight loss ever since. He now sees only blackness, except for a small area of a few degrees in diameter in the centre of his vision.

Choroideraemia is a genetic disease that leads to progressive degeneration of the retina in the eye. It generally affects males only and there is no treatment. The diagnosis is usually made in childhood and leads to blindness in men by their forties. It occurs due to deficiency of the REP1 gene located on the X chromosome.

The novel gene treatment was developed by Professor MacLaren in collaboration with Professor Miguel Seabra at Imperial College. It is designed to provide the gene missing in people with choroideraemia to stop the deterioration that gradually leads to blindness. It uses a virus essentially as a delivery vehicle that

ferries DNA, including the missing gene, into the right part of the eye. The virus has been engineered to infect the light-sensitive cells in the retina known as photoreceptors. There the gene is switched on and becomes active. With this particular gene therapy, the treatment could provide a one-off permanent correction of the disease because the gene is thought to remain in the retinal cells indefinitely.

"This trial represents the world's first ever attempt to treat this disease and is the first time that gene therapy has been directed towards the light-sensitive photoreceptor cells of the human retina," said Professor MacLaren. "This represents a major breakthrough and is highly significant for patients who are losing sight from other photoreceptor diseases, such as retinitis pigmentosa."

The trial will see 12 patients undergo surgery in which the gene therapy is injected into one eye. The other eye would then act as a control against which to assess any treatment effect. The researchers would, however, aim to go on to treat the second eye should the treatment prove to be effective. The aim of the trial is primarily to assess safety, but it will also gain initial data on how effective the treatment is. The researchers estimate that it will take two years to know whether or not the degeneration has been stopped completely by the gene therapy.

"While safety appears so far to be fine, the efficacy of the gene therapy will only be evident after 24 months," explained Professor MacLaren. "We need this time to measure any effect as the degeneration caused by choroideraemia is slow."

The clinical trial is funded by a grant awarded to the University of Oxford by the Department of Health and the Wellcome Trust, through the Health Innovation Challenge Fund.

Professor Seabra, who played a key role at Imperial College in identifying the gene causing choroideraemia and in eliciting the mechanism of cell death in the retina, commented: "The ability to offer a gene replacement treatment for these patients was the final objective of 20 years of intense research in my laboratory. This is a moment of fulfillment for us and a dream come true for all choroideraemia patients."

*Source: The Nuffield Laboratory of Ophthalmology.*

## **FURTHER GENE THERAPY SUCCESS**

Three US citizens who lost their sight in childhood have reported a dramatic improvement in vision after having gene therapy in both eyes. There was some improvement after the genetic fault in one eye was corrected four years ago. Now, one woman has described her joy at seeing her children's faces after her second eye was treated. Tami Morehouse, on regaining sight, said "Life's just so much easier at a level that most people take for granted. Yes, seeing my kids' faces - my son has big huge black eyes, my daughter has big beautiful blue eyes - I just can't tell you what that means."

The three have Leber's Congenital Amaurosis (LCA), which leads to severely impaired vision, involuntary eye movements and poor night vision. Several teams around the world are carrying out early trials of gene therapy in blindness, including experts at the Philadelphia Children's Hospital and the University of Philadelphia, US.

Only a handful of patients worldwide have received the treatment to boost a faulty gene underlying an inherited form of blindness. The research increases hope that gene therapy can

be used in a range of eye conditions.

The US researchers revealed in 2008 that 12 people with LCA had recovered some vision after being injected in one eye with an engineered virus carrying the gene RPE65. In a follow-up study they treated the other eye of three of them, and found it improved their sight even more. The subjects could see better in dim light and two were able to find their way around obstacles.

The results were revealed in the latest edition of the journal Science Translational Medicine. The principal investigator of the study, Dr Jean Bennett from the University of Pennsylvania, said the patients could now do things they could never do before, such as walk around at night, go shopping for groceries and recognise people's faces.

"We've shown that it is possible to safely treat both eyes of people with this particular form of retinal deficiency using a gene-based treatment", she said. "We've demonstrated that the brain understands what the retina is seeing. I think it will be a stepping stone to treating more common forms of blindness in both eyes."

The researchers now hope to treat the second eye of the remaining nine patients, and extend the clinical trial.

Commenting on the study, Clara Eaglen, policy and campaigns manager at the Royal National Institute of Blind People (RNIB), UK, said: "The early results of this small scale trial are encouraging, but clearly, a lot more research is needed to maximise the benefits of gene therapy techniques and understand how they can then be turned into effective treatments for a variety of more common degenerative eye conditions."

## **NEW SIGHT**

Fifteen years ago, the bid to create Australia's first bionic eye relied on university researchers pillaging old stereos for parts. But now, 154 researchers led by the University of NSW's biomedical engineers could be less than a year away from their task to save the vision of degenerative eye disease victims. In 1997, when the work began, Gregg Suaning and Nigel Lovell were unfunded but dogged researchers ripping old stereos asunder for spare parts in their attempts to build a bionic eye. Their work today is a \$42 million joint project between the university, the Bionics Institute, the Centre for Eye Research Australia, NICTA and the University of Melbourne to restore sight to the blind. Researchers say they could be months away from offering material hope to people with macular degeneration and retinitis pigmentosa, the leading causes of sight loss in industrial countries.

The technology revolves around an intricate and miniscule implant containing 98 electrodes, which is designed to stimulate nerve cells in the retina. Images taken by an external camera implanted in glasses worn by the patient would be processed and then relayed via an external wire to a receiver implanted behind the ear, from which signals will be sent to the retina processing chip. If all goes to plan the retina, having been stimulated with the signals, will send information via "visual pathways" to vision processing centres in the brain. Human trials will begin next year.

But they will not be offered to people with any vestiges of sight.

"Because they have so much to lose, people who even see light won't be able to qualify," Professor Suaning said.

The human trials of their bionic eye technology will be the first in Australia. The team began producing the implants last week, and will produce about 25 before they know whether they're ready to proceed further. It is envisaged the technology, and follow up treatment, will cost more than \$60,000 per patient — slightly more than the cochlear implant. The high cost will mostly be due to the cost of post-surgery treatment, and helping people make sense of the images they are seeing. It is one of two bionic eye development projects made possible by the allocation of \$50 million to bionic eye development. The other project is the Monash Vision Group.  
*Canberra Times*, 2 May 2012

## **TWO BLIND BRITISH MEN HAVE ELECTRONIC RETINAS FITTED**

Two British men who have been totally blind for many years have had part of their vision restored after surgery to fit pioneering eye implants. They are able to perceive light and even some shapes from the devices which were fitted behind the retina. The men are part of a clinical trial carried out at the Oxford Eye Hospital and King's College Hospital in London. The two patients, Chris James and Robin Millar, lost their vision due to RP. Up to a dozen British patients will be fitted with the implants.

The wafer-thin, 3mm square microelectronic chip has 1,500 light-sensitive pixels which take over the function of the photoreceptor rods and cones. The surgery involves placing it behind the retina from where a fine cable runs to a control unit under the skin behind the ear. When light enters the eye and reaches the chip it stimulates the pixels which sends electronic signals to the optic nerve and from there to the brain. The chip can have its sensitivity altered via an external power unit which connects to the chip via a magnetic disc on the scalp.

Chris James said there was a "magic moment" when the implant was switched on for the first time and he saw flashing lights - showing that the device was functional. "I am able to make out a curve or a straight line close-up but I find things at distance more difficult. It is still early days as I have to learn to interpret the signals being sent to my brain from the chip." Mr James, a motor-racing enthusiast, says his ambition is to be able to make out the silhouettes of different cars on the race-track.

Prof MacLaren, who fitted the first implant in the UK at the Oxford Eye Hospital, said: "It's the first time that British patients who were completely blind have been able to see something. In previous studies of restorative vision involving stem cells and other treatments, patients always had some residual sight. Here the patients had no light perception at all but the implant reactivated their retina after more than a decade."

The chip results in the brain receiving flashes of light rather than conventional vision - and it is in black and white rather than colour. But in an unexpected development, the other British man to have the implant says he is now able to dream in colour for the first time in 25 years. Robin Millar says he is also able to stand in a room and detect light coming through windows.

Prof MacLaren said the results might not seem extraordinary to the sighted, but for a totally blind person to be able to orientate themselves in a room, and perhaps know where the doors and windows are, would be "extremely useful" and of practical help.

Mr Tim Jackson, eye surgeon at King's College Hospital who has also fitted one of the devices, said: "This pioneering treatment is at an early stage of development, but it is an

important and exciting step forward, and may ultimately lead to a much improved quality of life for people who have lost their sight from RP. Most of the people who receive this treatment have lost their vision for many years, if not decades. The impact of them seeing again, even if it is not normal vision, can be profound, and at times quite moving."

The implants have been developed by a German medical technology company, Retina Implant AG. The British trial has been made possible by the company successfully obtaining approval to extend the year-long phase II human clinical trial of its retinal implant outside Germany, to five sites — Oxford, London and Budapest, along with two additional locations in Germany.

For those suffering with RP, Retina Implant's technology creates a small black-and-white window on the world, says Eberhart Zrenner, the company's co-founder and director and chairman of the University of Tübingen's Institute for Ophthalmic Research in Germany. Looking ahead, Zrenner hopes to widen patients' field of vision further. "Because our chip has independent miniature photodiodes, we could arrange three of them in a row beneath the retina," he says. The ability to produce accurate colours via retinal implants, however, is very complicated and may not be possible for years, he adds. Retina Implant has also developed an outpatient treatment for early-stage retinitis pigmentosa called Okuvision, which uses electric stimulation to help preserve retinal cells.

The phase II extension expands Retina Implant's trial to an additional 25 patients in 2012 and follows a partnership the company has struck with the Wills Institute in Philadelphia. Wills is looking to become the lead U.S. clinical trial investigator site for Retina Implant's technology and to help the company through the U.S. Food and Drug Administration's (FDA) review process.

"Cutting-edge technologies such as sub-retinal implants are typically at a disadvantage when seeking FDA approval due to the lack of a track record, but Retina Implant's work in Europe provides a precedent for the FDA to consider," says Julia Haller, Wills's ophthalmologist in chief. "There's information available to U.S. regulators about how patients have responded so far," she adds.

*Sources: Fergus Walsh, BBC News Health, 3 May 2012; Larry Greenmeier, Scientific American, 12 December 2011.*

## **PHOTORECEPTOR TRANSPLANT RESTORES VISION IN MICE**

Scientists funded by the UK Medical Research Council (MRC) have shown for the first time that transplanting light-sensitive photoreceptors into the eyes of visually impaired mice can restore their vision.

The research, published in *Nature*, suggests that transplanting photoreceptors – light-sensitive nerve cells that line the back of the eye – could form the basis of a new treatment to restore sight in people with degenerative eye diseases.

Scientists from UCL Institute of Ophthalmology injected cells from young healthy mice directly into the retinas of adult mice that lacked functional rod-photoreceptors. Loss of photoreceptors is the cause of blindness in many human eye diseases including age-related macular degeneration, retinitis pigmentosa and diabetes-related blindness.

There are two types of photoreceptor in the eye – rods and cones. The cells transplanted were immature (or progenitor) rod-photoreceptor cells. Rod cells are especially important for seeing in the dark as they are extremely sensitive to even low levels of light.

After four to six weeks, the transplanted cells appeared to be functioning almost as well as normal rod-photoreceptor cells and had formed the connections needed to transmit visual information to the brain.

The researchers also tested the vision of the treated mice in a dimly lit maze. Those mice with newly transplanted rod cells were able to use a visual cue to quickly find a hidden platform in the maze whereas untreated mice were able to find the hidden platform only by chance after extensive exploration of the maze.

Professor Robin Ali at UCL Institute of Ophthalmology, who led the research, said:

“We’ve shown for the first time that transplanted photoreceptor cells can integrate successfully with the existing retinal circuitry and truly improve vision. We’re hopeful that we will soon be able to replicate this success with photoreceptors derived from embryonic stem cells and eventually to develop human trials.

“Although there are many more steps before this approach will be available to patients, it could lead to treatments for thousands of people who have lost their sight through degenerative eye disorders. The findings also pave the way for techniques to repair the central nervous system as they demonstrate the brain’s amazing ability to connect with newly transplanted neurons.”

Dr Rachael Pearson from UCL Institute of Ophthalmology and principal author, said:

“We are now finding ways to improve the efficiency of cone photoreceptor transplantation and to increase the effectiveness of transplantation in very degenerate retina. We will probably need to do both in order to develop effective treatments for patients.”

Dr Rob Buckle, head of regenerative medicine at the MRC said:

“This is a landmark study that will inform future research across a wide range of fields including vision research, neuroscience and regenerative medicine. It provides clear evidence of functional recovery in the damaged eye through cell transplantation, providing great encouragement for the development of stem cell therapies to address the many debilitating eye conditions that affect millions worldwide.”

The researchers demonstrated previously, in another study published in *Nature*, that it is possible to transplant photoreceptor cells into an adult mouse retina, provided the cells from the donor mouse are at a specific stage of development - when the retina is almost, but not fully, formed. In this study they optimised the rod transplantation procedure to increase the number of cells integrated into the recipient mice and so were able to restore vision.

The research was funded by the MRC, the Wellcome Trust, the Royal Society, the British Retinitis Pigmentosa Society, Alcon Research Institute and The Miller’s Trust. Robin Ali is a senior investigator of the National Institute for Health Research and carries out research at the NIHR Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and

UCL Institute of Ophthalmology. Rachael Pearson is a Royal Society University Research Fellow.

### **BLOOD-DERIVED STEM CELL PROGRESS**

Scientists at the University of Wisconsin-Madison in the USA have reported success in developing retinal cells, including photoreceptor cells, from stem cells derived from human blood. The University website reports that "Many applications of laboratory-built human retinal tissues can be envisioned, including using them to test drugs and study degenerative diseases of the retina such as retinitis pigmentosa, a prominent cause of blindness in children and young adults. One day, it may also be possible replace multiple layers of the retina in order to help patients with more widespread retinal damage" The full story and a link to the University's own website can be found at:

<http://www.rpfightingblindness.org.uk/newsevent.php?tl=newsevents&newseventid=258>

### **AN INTERESTING QUESTION**

A member of Retina Australia (NSW) recently contacted the organization with an interesting question: "Will the future stem-cell treatment for retinitis pigmentosa be expected to benefit only newly-diagnosed RP or long-standing disease as well?"

RA (NSW) ran this by one of the members of RA's Scientific & Medical Advisory Committee and shares with you his reply.

"Stem cell research is of promise but is well behind other forms of treatment such as gene therapy and 'pharmacological' intervention (i.e., Vitamin A - although there is controversy relating to the efficacy of this to slow down RP, a recent report suggests it preserves cone function)\*. Other treatments using nerve growth factors and prostaglandin drugs to retard are progressing as clinical trials. A vitamin-A analog (QLT091001) is undergoing clinical trials for two mutations that cause Leber's and also RP (mutations of the RPE65 and LRAT). Prosthetic devices are being implanted worldwide (for end stage RP), including a trial that will be beginning in Australia.

"There are no clinical trials planned for RP using stem cells that I am aware of. The reason is that stem cell transplants have only worked in a small developmental window in a mouse model. In order for them to work, stem cells need to have access to the degenerating retina. Because of anatomical changes to the retina, there is considerable 'remodelling' making access to the remaining retina for stem cells difficult. Prof Ali's group successfully implanted stem cells in a mouse model of RP in that small window with some success (about 5-6 yrs ago). His group just published a paper showing impressive stem cell preservation and function in a model of congenital stationary night blindness (CSNB). The significance of this is that it occurred in adult retina. However, in CSNB, there is little photoreceptor loss and thus little remodelling. I am sure Prof Ali will outline more on this later in the year when he presents at the conference.

"Therefore, stem cells are more likely to be an option for those early in the disease process when there has been minimal retinal remodelling. Prosthetic devices are the option for late stage and other methods that are undergoing clinical trials now, are available for the mid-range of the disease. There appears to be something available or in clinical trials that cover all phases of the disease, something that was not present 15-20 years ago.

"Stem cells are in the 'proof of principle' phase and have not as yet achieved sufficient laboratory success to warrant clinical trials."

## **OMEGA-3 SLOWS DOWN RP PROGRESSION**

A report published in *Archives of Ophthalmology* reveals that adults with retinitis pigmentosa (RP) who took vitamin A supplements over a period of four to six years, showed slower decline in annual rates of distance and retinal visual acuities by consuming a diet rich in omega-3 fatty acids.

Visual acuity data from 3 human trials conducted from 1984 to 1991, 1996 to 2001 and 2003 to 2008, involving individuals with typical RP, were examined by Eliot L. Berson, M.D., of Harvard Medical School and the Massachusetts Eye and Ear Infirmary, Boston, and his team. In the current study, the team enrolled 357 individuals with the condition, who were all taking vitamin A palmitate (15,000 IU/d).

Results from the study revealed that the mean (average) annual rate of decline in distance visual acuity was 40% slower among participants who consumed a diet high in long-chain  $\omega$ -3 fatty acids ( $\geq 0.20$  g/d), compared with participants whose diet was low in omega-3 fatty acids.

In a previous study, the team revealed that dietary omega-3 intake had an effect on retaining central visual field sensitivity. They found that individuals receiving omega-3 intake of at least 0.20 g/d, in conjunction with vitamin A palmitate, 15,000 IU/d had nearly a 50% slower rate of decline in central visual field sensitivity than patients receiving a lower omega-3 intake and the same dose of vitamin A.

They conclude:

"Therefore, the treatment regimen of vitamin A combined with an omega-3-rich diet ( $\geq 0.20$  g/d) should make it possible for many patients with typical RP to retain both visual acuity and central visual field for most of their lives."

Commenting about the rate of decline in letters per year on Early Treatment Diabetic Retinopathy Study (ETDRS) distance acuity testing, the researchers explain that the mean rate of decline in letters per year was 0.59 letter for individuals receiving high omega-3 intake, combined with vitamin A, compared to 1.00 letter for individuals receiving low omega-3 intake, combined with vitamin A, over a 4 to 6 year period.

The researchers estimate:

"A representative patient who starts receiving vitamin A by age 35 years and eats an omega-3-rich diet (i.e. one to two 3-ounce servings of oily fish per week) with an ETDRS acuity of 50 letters (equivalent to 20/30 on the Snellen chart) would, on average, be expected to decline to an ETDRS acuity of 24 letters (equivalent to 20/100 on the Snellen chart) at age 79 years, whereas this patient receiving vitamin A with a low dietary omega-3 intake (e.g. less than one 3-ounce serving of oily fish per week) would decline to this level at age 61 years."

Source: *Grace Rattue, Medical News Today, 16 February 2012.*

## ABOUT US

Retina Australia (ACT) Inc. is a member of the national body, Retina Australia (RA). Other members of RA are Retina Australia (NSW), Retina Australia (VIC) – which incorporates activities in Tasmania – Retina Australia (QLD), Retina Australia (SA) and Retina Australia (WA). There is also a newly-formed group in the Northern Territory.

Our role, and that of our fellow organisations, is to provide information and support to people and families affected by Retinitis Pigmentosa and other retinal dystrophies. We also raise funds for scientific research into the causes and prevention of these dystrophies.

Retina Australia is a member of Retina International, which has members and affiliates in more than 50 countries. It is estimated that more than 20 million people worldwide are affected by some form of retinal dystrophy.



FIGHTING BLINDNESS

**Mission Statement:** To provide information and support to people and families affected by inherited retinal dystrophies, and, with the support of the Australian community, to raise funds to finance scientific research into the causes, prevention and cure of retinitis pigmentosa.

### Ways You Can Help Retina Australia (ACT)

There are many ways you can help and support us. Listed below are some suggestions.

1. Suggest to family and friends that they hold a special event (such as a sponsored walk or fundraising dinner) to support our work.
2. Include a reference to us when updating your Will.
3. Continue with your much-appreciated cash donations.
4. Tell your local eye professionals (and your family and friends) if you have found the information provided by Retina Australia (ACT) and its support services useful.
5. Offer your services to a member of the executive as there are numerous small jobs that need to be done. Many of these do not require you to be on a committee.
6. If approached, consider allowing your medical information and DNA to be stored on the inherited retinal diseases database so it is readily available to eye researchers both here and overseas.
7. When you hear that someone in your community has been diagnosed with sight loss tell them about Retina Australia (ACT) and the support services offered.

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### Last Word

Whatever the goal we're pursuing  
No matter how rugged the climb  
We're certain to get there by trying our best  
And taking one day at a time  
'Forever' is hard to imagine  
'The future' may seem far away –  
But every new dawn brings a wonderful chance  
To do what we can on that day

Emily Mathews, Poet