



I-C

Newsletter for Retina Australia (ACT) Inc

EDITION 1/2014

February

Message from the President

Welcome to the first edition of I-C for 2014, with the best wishes of all committee members. We should also like to thank everyone who supported our major fundraiser at the end of 2013.

Contained within is a report of the fundraiser, together with some interesting research reports.

ROBIN POKE AM
President
Retina Australia (ACT)

Retina Australia (ACT) is proudly
sponsored by

Elders Real Estate Belconnen

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Phone: 02 6251 2088
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Website: eldersbelconnen.com.au

MEMBERS' "MONTHLY LUNCH DATE"

Where: Café Charisma
Shop 4
2 Colville Street
North Lyneham

Date: 2nd 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:

2014 Please let me know if you have a problem with transport and I will try to arrange for someone to pick you up.

Jan James
Secretary
Ph 6258 4823
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ANOTHER SUCCESSFUL FUNDRAISER

Lyn Mills

Canberra Times/Lifestyle

The annual spring racing fundraising luncheon for Retina Australia ACT was a colourful gathering with all the trappings of a day at the races, but I didn't see one horse.

Not unusual perhaps as the social side of racing is what gets people to the track. And as a fundraiser it works a treat.

Retina Australia ACT has a perfect spokesman for its organisation in their president Robin Poke. His tireless efforts, great sense of humour and no nonsense get on with it attitude is how he copes with this insidious disease that is not painful – unless you're bumping into things – is not contagious, life threatening or infectious but is debilitating to various degrees over a long period of time.

Robin Poke's diagnosis was made in England after his rugby mates complained he was tackling them as opposed to the opposing team and thus began a lifetime of coping.

He calls himself lucky as his RP has caused slow contracting of his sight. His coping mechanisms are effective and considerate of those around him as his peripheral vision diminishes. But his friends know how to get his attention and his three daughters and their partners keep an eye on him. He's fit.

Running marathons, rowing- because you don't have to look where you're going – and continues his commitment to the Olympic movement in many and varied capacities. He's a journalist, a sports administrator, competitor and author with encyclopaedic knowledge of rowing and was a Canberra finalist in the 2011 Senior Citizen of the Year.

But RP is a little organisation in a big field looking for funds for research, treatment, a cure and support for sufferers with genetic research at the heart of so many breakthroughs discovering thus far 100 mutant genes responsible for degenerative vision loss, then there's stem cell research and of course the bionic eye that has seen great progress and all will probably be part of the equation.

In the meantime life looks good for Robin Poke as he's going to be grandfather soon and one little baby is going to get a very up close and focused grandpa face to look at.



ANOTHER SUCCESSFUL FUNDRAISER (cont)

Retina Australia ACT's fifth consecutive annual fundraiser at Thoroughbred Park on 17 November last proved to be another fabulous afternoon of racing, tipping competitions, raffles and auctions. Attended by no less than 156 supporters, a record total of \$7045.35 was raised for research into a for cure retinal dystrophies.

The president of Retina Australia (ACT), Robin Poke, thanked attendees for their support and generosity, and gave them an overview of the organisation's role and function. He also explained how those with inherited genetic retinal disease manage their lives. Robin reported, too, on research progress in the areas of stem cell research, gene therapy and the bionic eye, and on the work being done by those involved with the Inherited Retinal Diseases Register and DNA Bank at Sir Charles Gairdner Hospital, Perth.

As usual, the polished and urbane David Kilby kept things ticking over by way of his usual wit and mischief, while special mention should be made of the contribution made by our Secretary, Jan James, the major organiser of the fundraiser, whose contribution was awe-inspiring.

We also owe a huge debt to Women in Racing, who for five years now have lent us unstinting support, and to the many generous sponsors, who provided us with a wonderful range of products and without whom the amount raised would have been far smaller. The major auction prize, a special edition centenary number plate, was donated by the ACT government and brought the top bid of the day.

The list of sponsors is hereunder. Please support those who support us.

Last Stop Ambledown Brook, David and Jenny Kilby's famous Bed & Breakfast in the Hills of Hall.

Cataldo's Hair Salon, Melbourne Building Canberra City

Mee Sing, Chinese Restaurant, Lyneham

Christmas Hampers x 4 including homemade Christmas cake, shortbread, liquer chocolate balls and marmalade, made by Jan James, Margaret Freeman and daughter Ruth and lastly Mavis Bird

Shaw Vineyard Estate, "Cielo" Sparkling Semillon

Murrumbateman Country Inn, two course dinner for two

Flint In The Vines, \$50 gift voucher

DREAM DESIGN, \$200 Gift Voucher

DREAM DESIGN, Cushions

FASCINATORS, made by Barbara Burton Millinery

Priceline Bungendore, two boxes of Chocolates

Rachel Wallace, Set of Ceramic Bowls

Harris Scarfe, Belconnen Mall – Gabriel Gate's 6-piece knife set

Harris Scarfe, Belconnen Mall - Rona Champagne Flutes

Pankhurst Wines from the Hills of Hall district, Celebrating 25 years of winemaking

RESEARCH REPORTS

Stem Cells

Protein breakthrough

A friend of Retina Australia (ACT)'s Secretary, Jan James, sent her the following information, published by London's *Daily Telegraph*:

Thousands of people suffering from common forms of blindness could have their sight restored by a pioneering treatment. Researchers at Oxford University have discovered that by replacing a missing protein in the retina they can prevent cells from degenerating. With results that have "surpassed expectations" the therapy even improves the sight of those who have already begun to go blind. Two men who were already at an advanced stage of vision loss have had "dramatic improvements" in their sight which, so far, have lasted for two years.

Robert MacLaren of the Nuffield Laboratory of Ophthalmology at the University of Oxford, said: "We're absolutely delighted with the results so far. In truth, we did not expect to see such dramatic improvements. This has huge implications for anyone with a genetic retinal disease such as age-related macular degeneration or retinitis pigmentosa because it has, for the first time, shown that gene therapy can be applied safely before the onset of vision loss."

The trial was carried out on patients suffering from choroideremia - a rare, inherited cause of blindness that affects about one in 50,000 people. It is caused by a defective gene that fails to produce REP-1 - a protein needed to keep pigment cells in the retina healthy. Without it, the cells slowly stop working, switch off and die. The scientists found that the protein could be replaced in the eye by inserting it into the DNA of a harmless virus, which can be injected into cells beneath the retina. As the virus "infects" these retinal cells, the missing protein is restored.

"The purpose of our trial is to put this missing protein back into the retinal cells and prevent further degeneration," Professor MacLaren said. "We're not talking about treatment that needs to be repeated; we're talking about a single one-off replacement of the gene."

The results are published in the authoritative medical journal *The Lancet*.

Bionic Eye Projects in Melbourne

Last year the Australian Research Council (ARC) announced it would continue to fund the research of the Monash Vision Group and Bionic Vision Australia, which are developing different but complementary bionic eye technologies. Bionic Vision Australia's research program for 2014 will build on current patient tests to further develop the Wide-View and High-Acuity devices, with engineers and surgeons working through an iterative design and testing process. This work is essential preparation for the next set of patient tests with next generation devices. The Monash Vision Group has unveiled the prototype Gennaris wireless device - a direct to brain bionic eye which will assist patients with a damaged optic nerve. The funding continuation will allow further development and refinement of the device ahead of patient trials next year. Source: www.bionicvision.org.au

Tackling The Next Gene Therapy Challenge: Autosomal Dominant Diseases

At a recent meeting of the North American Foundation Fighting Blindness in Las Vegas, Al Lewin, Ph.D., of the University of Florida, discussed progress in tackling the vexing problem of developing gene therapies for autosomal dominant retinal disease — specifically retinitis pigmentosa (RP) caused by mutations in the gene rhodopsin (RHO).

Using human-engineered viruses to deliver healthy DNA to replace defective, disease-causing DNA in retinal cells is a cutting-edge technique that's still at an early stage of clinical development. However, recessive gene therapies involve a relatively straightforward, one-step approach: replace the defective gene which is not functioning.

Treating autosomal dominant retinal diseases is a more formidable challenge, because researchers need to deal with one gene copy expressing a toxic protein and another that's functioning normally.

"For dominant disease, we may need to silence the expression of the mutated gene in addition to delivering a normal copy. We may need a two-step process," says Dr. Lewin. "It's complicated, because we have to suppress the mutated gene, in our case RHO, without having a secondary effect on other genes with the silencing agent."

While the knock-down and replace strategy is a focus for his team, Dr. Lewin says that a one-step approach might still be viable in some cases. He discovered that just overriding the mutant gene with a healthy gene might sometimes do the trick.

"We found, in the course of our studies, that two steps might not be necessary for some RHO mutations. We might only need to deliver a normal copy of RHO to suppress the effect of the mutant," he says. "It is probably a matter of shifting the balance towards having more normal RHO than abnormal to preserve photoreceptors, slow down the degeneration significantly and retain sight."

"You can think of the two gene copies as being like radios. One plays The Beatles and the other plays static," explains Stephen Rose, Ph.D., chief research officer of the Foundation. "If you can play The Beatles loud enough, you might be able to override the static so it isn't noticeable. However, you can't play The Beatles too loud or you'll hurt your ears."

In 2011, Dr. Lewin, along with Marina Gorbatyuk, Ph.D., and William Hauswirth, Ph.D., his collaborators at the University of Florida, were honored with the Foundation's Board of Director's Award for discovery of the override technique.

Genable, a gene development company in Ireland, is also taking on the challenge of developing gene therapies for autosomal dominant retinal diseases. "We are focused on moving the most promising forms of treatment into a clinical trial as soon as we can," says Dr. Lewin. "We appreciate the generous support of the Foundation for this important translational work, and we understand the urgency to get it out to the patients."

RP Gene Therapy Improves Vision After Significant Retinal Degeneration

Dec. 30, 2013 – A Foundation-funded research team has developed a [gene therapy](#) that restored vision in mice which had lost half of their photoreceptors to autosomal recessive retinitis pigmentosa (arRP) caused by mutations in the gene PDE6 α . Results of the study, led by [Stephen Tsang](#), M.D., Ph.D., of Columbia University, were published in the journal [Human Molecular Genetics](#).

Thanks, in part, to this advancement, an international consortium led by [Bernd Wissinger](#), Ph.D., of the University Eye Hospital Tübingen in Germany, was recently formed to move PDE6 α gene therapy into a clinical trial.

Previously, a team led by Dr. Tsang showed that gene therapy [improved and preserved vision in mice with an early stage of PDE6 \$\alpha\$ -associated arRP](#) before photoreceptor degeneration had occurred. The treatment prevented photoreceptor degeneration for the length of the study, which was 11 months, about half the lifespan of the mice.

However, Dr. Tsang says that most people with arRP caused by PDE6 α mutations exhibit the loss of many photoreceptors when they are first examined by an eye-care professional, usually in their late teens or early twenties. Therefore, a human gene therapy for this disease needs to work after significant degeneration has occurred.

His team's study of PDE6 α gene therapy in mice with mid-stage retinal degeneration resulted in preservation of remaining rods, the photoreceptors responsible for peripheral and night vision, and cones, the photoreceptors that provide central vision and the ability to perceive details and colors. Improvements in retinal sensitivity — as measured by an electroretinogram, or ERG — persisted for six months, the length of the study.

PDE6 α expresses a protein in rods that plays a key role in phototransduction — the process of converting light into electrical signals sent to the brain, where they are interpreted as vision. In people with most forms of RP, including those caused by PDE6 α mutations, the loss of rods eventually leads to degeneration of cones.

Dr. Tsang's gene therapy was contained in a tiny drop of liquid injected underneath the retinas of the mice. The liquid consisted of healthy copies of PDE6 α , which were inserted into a human-engineered adeno-associated virus, or AAV. The AAV was designed to safely and effectively deliver the therapeutic genes into the rods of the mice. AAVs have also performed well thus far in [several gene-therapy clinical trials for retinal diseases](#).

“We are very pleased that Dr. Tsang showed his treatment has potential to work for a stage of disease that is applicable to humans,” says Stephen Rose, Ph.D., chief research officer, Foundation Fighting Blindness. “The knowledge gained from his lab research moves us an important step closer to a clinical trial.”

The Australian IRDR and DNA Bank

Introduction

This is a status report for the resource "The Australian Inherited Retinal Disease (IRD) Register and DNA Bank" as at August 2013.

The custodian for this resource is the Department of Medical Technology and Physics, Sir Charles Gairdner Hospital, Western Australia.

The creation and development of this resource has been made possible by the generous funding from Retina Australia (WA) (since 1984), Retina Australia and Retina Australia (South Australia), and by the continued support of Sir Charles Gairdner Hospital.

The purpose of this project is to establish and maintain a public and enduring Australian resource for use by approved scientists and clinicians embarking on inherited retinal disease research, including those undertaking clinical trials and (in the future) offering therapies. The resource consists of (1) a register of consenting Australians affected with an IRD and their family members, and (2) a DNA bank containing DNA from consenting individuals.

Information within the register includes detailed results of electrophysiology tests, psychophysical measurements and ophthalmic examinations, demographic information, family and clinical data (best known diagnosis being a crucial item), and details of genetic analyses undertaken and genetic information gathered, including the defect causing the disease within each family where this has been established.

Information and DNA held within this resource may be made available to approved scientists and clinicians upon request. Information that may identify an individual will not be released without prior negotiation with the individual, and only if he or she chooses to become involved.

Project Staff Staff funded by Retina Australia and directly involved with the IRD register and DNA bank on a day-to-day basis are Tina Lamey (Senior Research Scientist), Ling Hoffmann (Research Assistant), Hannah Montgomery (Research Scientist), and Caitlyn Kap (Research Assistant). Departmental staff directly involved with the project include Dr John De Roach (Principal Medical Physicist) and Terri McLaren (Senior Medical Scientist).

Other departmental staff noted as co-investigators on the project's SCGH Human Research Ethics Committee application are Enid Chelva (Clinical Physicist Manager), Sarina Laurin (Senior Medical Scientist) and Monika Dolliver (Senior Medical Scientist).

Professor David Mackey, Dr Alex Hewitt, Professor Ian Constable and A/Professor Pirooska Rakoczy of the Lion's Eye Institute also have involvement with this project, and are noted as co-investigators, as is A/Professor Roger Price, Head of the Department of Medical Technology and Physics, Sir Charles Gairdner Hospital.

A/Professor Robyn Jamieson (Children's Hospital at Westmead and the Children's Medical Research Institute, NSW) and A/Professor John Grigg (Sydney Eye Hospital and the Save Sight Institute, NSW) are also co-investigators for this project.

Significant and valued assistance is provided by the department's reception, secretarial, purchasing, information technology and other staff.

Ethics and Quality Assurance

Approval for this project was granted by the SCGH Human Research Ethics Committee on 25th May 2001.

This project is carried out according to international standards with regard to its quality measures (ISO9001:2008). All relevant procedures, work instructions, records and standard forms and letters are kept in accordance with the ISO9001:2008 accredited quality documentation system. All associated processes are subject to both internal and external audit every 12 months.

DNA Collection

Table 1 shows (a) the number of participants and families with information recorded in the register, and (b) the number of participants and families with information recorded in the register and with DNA stored in the DNA bank, from 2006 until now.

Table 1: Statistics relating to the numbers of individuals and families currently held in the database.

| | Aug2 006 | Aug2 008 | Aug2 010 | Aug2 011 | Aug 2012 | Aug 2013 |
|------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Participants in register | 1285 | 1680 | 2854 | 3671 | 5129 | 5611 |
| Families in register | 735 | 882 | 1230 | 1484 | 1926 | 2078 |
| Participants per family | 1.75 | 1.90 | 2.32 | 2.47 | 2.67 | 2.70 |
| Participants with DNA stored | 444 | 724 | 1728 | 2461 | 3754 | 4210 |
| Families with DNA stored | 214 | 323 | 631 | 846 | 1195 | 1329 |

Table 1 shows that for the one year period August 2012 to August 2013 the number of subjects for whom information has been recorded in the register has increased from 5129 to 5611, an increase of 482 subjects. The number of DNA samples stored has risen from 3754 to 4210, an increase of 456 samples.

Note that the average number of participants in each family has steadily risen from 1.75 in 2006 to 2.70 in 2013. This is probably attributable in part to an increasing emphasis on gathering information from an entire family, rather than from individual participants, as this project has matured.

Included in the figures in Table 1 are DNA samples stored for 95 non-related individuals with no known family history of retinal disease, and deemed normal following ophthalmic and electrophysiology testing. This DNA is used as control DNA.

Table 2 shows the distribution of DNA collection by place of origin. The 'Unassigned Mackey' DNA originates mainly from Tasmania and Victoria, but the details are yet to be documented.

Table 2 Number of individuals on the register and number of DNA samples in the DNA bank by place of origin.

| Origin | No. DNA samples |
|--------------------------|------------------------|
| ACT | 57 |
| NSW | 783 |
| NT | 10 |
| QLD | 385 |
| SA | 245 |
| TAS | 37 |
| VIC | 572 |
| WA | 1389 |
| Unassigned Mackey DNA | 658 |
| International/Unassigned | 74 |
| TOTAL | 4210 |

Table 2 shows that 33% of all DNA has been collected from Western Australians. DNA has been being collected from Western Australians since 2001, and the DNA bank became a national resource in 2009. A long-term goal of this project is to have each of the states and territories represented on a population basis to at least the level at which Western Australia is currently represented.

Figure 1 gives a breakdown of stored DNA by clinical diagnosis, for affected and carrier subjects only. Genetic analysis projects are underway for diagnostic cohorts representing 90% of all DNA stored (i.e. all shown except 'other').

Figure 1 DNA samples collected from affected or carrier subjects, by diagnosis

| Diagnosis | DNA samples |
|------------------|--------------------|
| RP | 1029 |
| Stargardt | 251 |
| Macular/Pattern | 187 |
| Other | 169 |
| Usher Syndrome | 150 |
| Cone/Cone-Rod | 134 |
| LCA | 48 |
| Bardet-Biedl | 40 |
| Retinoschisis | 37 |
| Choroideraemia | 26 |

Genetic Analysis

Genetic analysis performed to date has been carried out by (a) Sanger sequencing, (b) (whole exome or targeted) next generation sequencing (NGS), (c) (whole or targeted) exome mutation array, or (d) genotyping microarray.

So far, some form of genetic analysis has been carried out on 32% of all DNA samples stored from affected or carrier participants, and the probable disease-causing variant has been identified in 48% of these analyses.

Table 3 indicates the number of participants who have had one or more IRD-causing mutations identified, tabulated by affected gene.

This table includes 210 participants whose IRD is highly likely of recessive inheritance. Of these 210 participants, two IRD-causing mutations were identified on the same gene in 105 cases, and an IRD-causing mutation was established homozygously for a further 15 participants. For the remaining 90 participants, either an existing second IRD-causing mutation in the same gene was not detected by the analysis method used, or the single IRD-causing mutation detected was not in the gene causing the IRD in that individual.

Table 3 Occurrences of genes in which disease-causing mutations have been identified.

| Gene | Occurrences | Participant clinical diagnoses |
|-------------|--------------------|--|
| ABCA4 | 108 | Stargardt, cone-rod, ukRP |
| BBS2 | 1 | BBS |
| BBS5 | 1 | BBS |
| BBS7 | 1 | BBS |
| BEST1 | 8 | Best, ARB, Stargardt |
| CACNA2D4 | 1 | cone-rod |
| CEP290 | 2 | LCA |
| CHM | 28 | choroideraemia |
| CRB1 | 16 | arRP,ukRP, LCA |
| CYP4V2 | 1 | cone-rod |
| EFEMP1 | 5 | Dominant drusen, Doyne's, Malat, Leven |
| GPR98 | 1 | BBS |
| GUCY2D | 1 | LCA |
| IGH3B | 1 | adRP |
| LRP5 | 1 | BBS |
| MTND1 | 1 | LHON |
| MTND4 | 1 | LHON |
| MY07A | 6 | Usher, BBS |
| NMNAT1 | 2 | LCA |
| NR2E3 | 3 | arRP |
| NRL | 1 | adRP |
| OPA1 | 1 | DOA |
| PDE6A | 1 | ukRP |

| | | |
|----------|----|-----------------------|
| PDE6B | 8 | arRP,x1RP,ukRP |
| PROM1 | 5 | arRP,x1RP,ukRP |
| PRPF3 | 7 | adRP |
| PRPF31 | 1 | adRP |
| RDS | 4 | adRP, Bests, cone-rod |
| RHO | 7 | adRP |
| RP1 | 15 | X1RP,adRP |
| RP9 | 1 | adRP |
| RPE65 | 1 | LCA |
| RPGR | 20 | X1RP,ukRP,LCA |
| RPGRIP | 2 | ukRP |
| RSI | 15 | Retinoschisis |
| SNRNP200 | 1 | BBS |
| SPATA7 | 1 | LCA |
| TIMP3 | 1 | Sorsby's |
| USH2A | 60 | Usher,ukRP,arRP,BBS |

(ukRP = RP of unknown inheritance)

LED lights ruin retinas, researchers say

A study by Spanish researchers found that eco-friendly LED lights can be damaging to your retinas, which cannot re-grow or be replaced. The lights produce high levels of radiation in the "blue band" of the light ray rainbow, which, over time, can damage retinas, Think-Spain reported.

Dr. Celia Sanchez Ramos, an investigator at Madrid's Complutense University, said the retina -- a highly sensitive tissue covering the eye -- can never re-grow itself or be replaced once it has become damaged.

Sanchez Ramos said damaged retinas are likely to become an epidemic sometime soon because of the use of computer, mobile phone and TV screens, and even traffic lights and street lights, which have been gradually replaced with LED technology.

"This problem is going to get worse, because humans are living longer and children are using electronic devices from a young age, particularly for schoolwork, instead of paper," Sanchez

Ramos said. "Eyes are not designed to look directly at light -- they are designed to see with light."

However, people can fight the effects of the dangerous rays by wearing "adequate protection," and by closing "our eyes often to soften the impact."

Adding foods to your diet that are rich in vitamin A, such as spinach and peppers, will protect the eyes, Ramos said.

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).

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.

Congratulations from all of us in the ACT

This is to advise that Graeme Banks our National President and his wife Lynette celebrated their 50th wedding anniversary at Old Government House, Parramatta on 8th February with 96 persons present.

When sending out the invitations they indicated no presents but, if the invitee wished a donation to Retina Australia would be welcomed. Without the on-line donations the wonderful total of \$10,360 was received.

We send them our heartfelt congratulations.

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