AUSTRALIAN & NEW ZEALAND
REGISTRY OF ADVANCED GLAUCOMA

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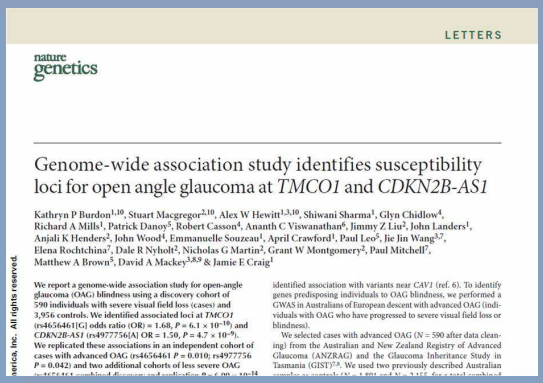
WORLD FIRST DISCOVERY

It certainly has been an exciting 12 months. Thanks to your assistance the Australian and New Zealand Registry of Advanced Glaucoma has recently discovered two new genes that are associated with the increased risk of developing severe open angle glaucoma.



LETTERS

nature genetics

Genome-wide association study identifies susceptibility loci for open angle glaucoma at *TMCO1* and *CDKN2B-AS1*

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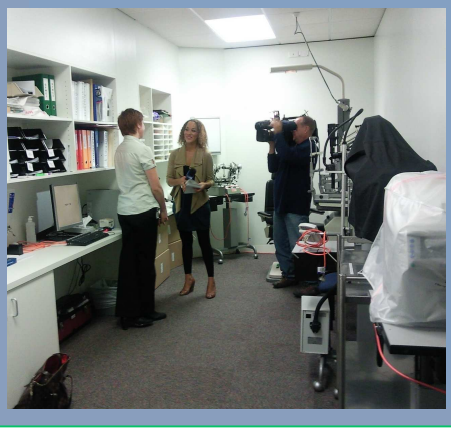
We report a genome-wide association study for open-angle glaucoma (OAG) blindness using a discovery cohort of 590 individuals with severe visual field loss (cases) and 3,956 controls. We identified associated loci at *TMCO1* (rs4656461[G] odds ratio (OR) = 1.68, $P = 6.1 \times 10^{-10}$) and *CDKN2B-AS1* (rs4977756[A] OR = 1.50, $P = 4.7 \times 10^{-9}$). We replicated these associations in an independent cohort of cases with advanced OAG (rs4656461 $P = 0.010$; rs4977756 $P = 0.042$) and two additional cohorts of less severe OAG

identified association with variants near *CAV1* (ref. 6). To identify genes predisposing individuals to OAG blindness, we performed a GWAS in Australians of European descent with advanced OAG (individuals with OAG who have progressed to severe visual field loss or blindness).

We selected cases with advanced OAG ($N = 590$ after data cleaning) from the Australian and New Zealand Registry of Advanced Glaucoma (ANZRAG) and the Glaucoma Inheritance Study in Tasmania (GIST)[7,8]. We used two previously described Australian

The world-first findings were published online in the prestigious *Nature Genetics* journal on May 1st, 2011 in an article titled "Genome-wide association study identifies susceptibility loci for open angle glaucoma at *TMCO1* and *CDKN2B-AS1*".



Dr Kathryn Burdon, from Flinders University, was interviewed by Channel 9 news regarding the findings of the study. The story went to air on Wednesday May 4th and created great awareness of the work being done through the registry.

The findings are likely to lead to better screening opportunities and more effective treatment for people who may be at a higher risk of developing open angle glaucoma.

GREAT RESPONSE

We have had a wonderful response to the "Participants' Questionnaire 2010". Thank you so much to everyone who took the time to provide some additional information to the registry. We have been able to complete lots of missing data and also collate new information that is being analysed by members of our team.

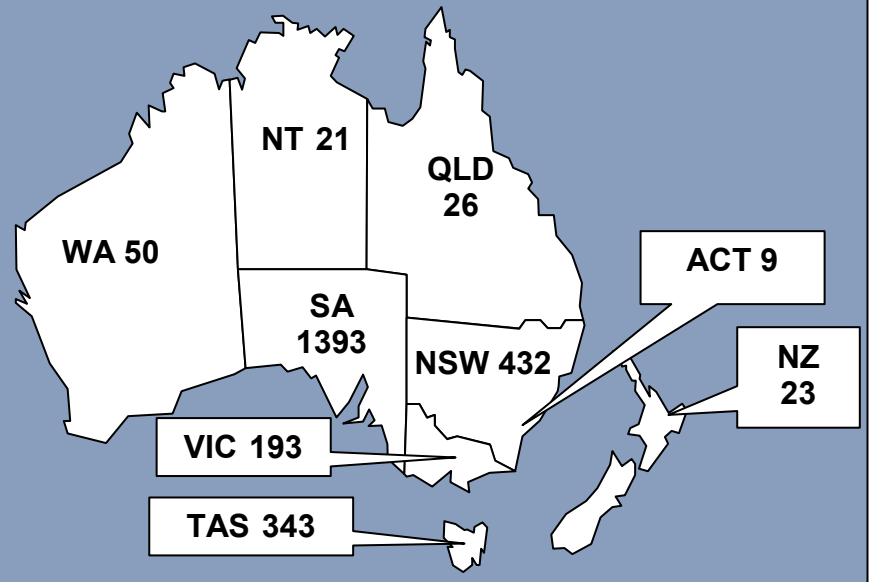
A big thank you must also go to the generous people who have either made a donation or asked to be contacted regarding making a donation. We have received gifts directly to the registry and also through donations made to our funding body, the Eye Foundation.

The information gathered through the survey, such as your family's ethnic background, can be an important part of determining a picture of how an eye disease is inherited. Some subtypes of glaucoma occur more commonly in some cultural groups, such as pseudoexfoliation in Scandinavian communities. Some gene mutations (changes) may also be found to be specific to a particular ethnic group.

Thank you for sharing your journeys with us. The anecdotal information you provided will help us to take an overall view of how a person progresses through to the advanced stages of glaucoma and what the contributing factors may be.

It's still not too late to send in your questionnaire. If you need a new form or envelope please contact our office (see back page).

Glaucoma blood samples and referrals continue to be received from every state and territory of Australia and from New Zealand.



Follow-up and Compliance:

We can not control the genes we inherit or the impact they may have on us over time. It is vitally important that when we can control something that could affect our eyesight, that we take the time and make the effort to do so.

According to Glaucoma Australia, over 10% of vision loss due to glaucoma may be caused by non-compliance with medication. Their website also estimates that at least one third of glaucoma patients will go from being "occasionally" non-compliant to "often".

A few of our participants reported to episodes of non-compliance at some stage during their glaucoma journey. Moving house or suffering other medical problems can cause complications with administering medication and can also cause lack of follow-up with a specialist. These incidences can allow time for glaucoma damage to progress.

Interesting facts…..

- The youngest participants in the registry have been diagnosed at birth or in their first few months of life. These participants have primary congenital glaucoma.
- Our oldest (confirmed) participant is 99 years of age and was recruited at 99 years of age. She was diagnosed at the age of 93.
- Although the project recruits from Australia and New Zealand wide, through our cascade screening programme we have also collected samples from India, France, Denmark and the UK.
- At least one participant has recorded eleven members of their extended family who have been affected by glaucoma. The relatives span three generations of the one family.

Genetic testing can help prevent vision loss from glaucoma

Example: Testing the *Myocilin* gene

As part of the registry, we offer genetic testing to individuals with severe glaucoma. Finding a gene change in their *Myocilin* gene means that other people in the family can have it too, and are at risk of having glaucoma.

As a result, through the registry, we offer screening to these individuals' family members so that they can learn more about their risk of developing the condition. Those who carry the same familial gene change have a very high risk of developing glaucoma in their lifetime, but they can now benefit from early interventions to prevent or minimise visual loss from glaucoma.

On the opposite side, those who do not carry the familial *Myocilin* gene change have a risk of developing glaucoma that is roughly the same as the general population.

So far we have been contacted by 48 individuals across Australia who have requested to be screened for their known familial mutation.

A number of these people would have probably lost some vision due to glaucoma later in life, but they are now able to act on it earlier with appropriate interventions and management.

The Australian Childhood Vision Impairment Register

We have partnered with The Australian Childhood Vision Impairment Register, which is sponsored by the Royal Institute for Deaf and Blind Children, in partnership with children, families, teachers, health professionals and low vision service providers.

The Register is the first of its kind in Australia, and is capturing uniquely Australian data on children with vision impairment. This data will be used to improve services for children and by researchers who work in the area of eye disease and disorders of vision.

Families are warmly invited to register their children. The age range is from 0-18 years, with any eye condition that causes vision impairment in both eyes.

Families can access the website to begin the registration process at: http://www.vifamilynetwork.org.au

The criteria for being included on the Register are available on the website, and if families are unsure, they can email or call Register staff, who will help out. Their phone number is (02) 9872 0303.

The VI Family Network website provides families with low vision resources and news of upcoming events. There is also access to an online parent forum for families with registered children, where parents can meet, chat, share ideas and support one another.

If you have a child with vision impairment we hope that you will consider joining this important Register.

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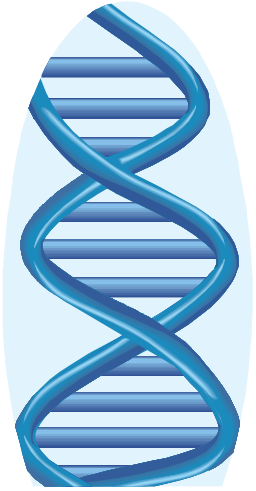
vifamilynetwork.org.au

Question of Ethnicity:

Why do we ask for your cultural heritage and that of your parents? We are all the products of genes that have been passed down from our parents, and from their ancestors. Not only can we inherit physical traits such as eye colour, hair colour, skin tone and height from our ancestors, we can also inherit mutations in our DNA. Some of these mutations can be passed on with no consequence and others may have the potential to cause harm.

Genes from our ancestors may have been passed on, through many generations and this is important to know as some diseases are common in particular ethnic backgrounds. For example, previous studies have found that the eye condition of pseudoexfoliation has a higher prevalency amongst Scandanavian populations (eg Krause et al, (1988) in Acta Ophthalmol (Copenh) 184 (Suppl: 120–122), stated that it was found in 21% of the population aged above 59 years in Finland).



For these reasons, information on your ethnic background (including the background of your parents) can contribute valuable insight into what genetic changes you may be susceptible to. It may also allow us to add valuable data to other research projects looking at the causes of certain eye diseases.

We have recruited participants from a very diverse range of ethnic groups. From the information available, countries of origin include such examples as; Bulgaria, Chile, China, Czechoslovakia, Finland, Ghana, Hungary, Ireland, Lebanon, Malta, Nigeria, the Philippines, Poland, Russia, Scotland, Spain, Sri Lanka, Vietnam, Wales and Zimbabwe.

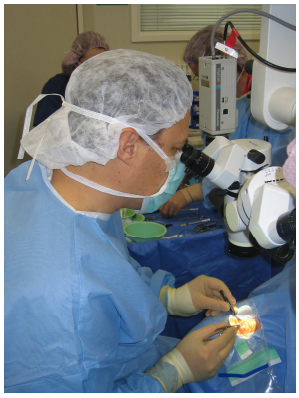
We have had some participants who have reported themselves as “Australian” with no further clarification. Although we may assume they could be of British or European descent we can never be 100% sure and therefore they fall into the “Unknown” category.

Terminology:

- **Anterior Segment Dysgenesis (ASD):** The anterior chamber of the eye is the front part consisting of the cornea, iris and lens. When a part of this segment of the eye does not develop properly a patient is considered to have an anterior segment dysgenesis. There are a number of conditions that fall into this subtype of glaucoma including: Rieger's Anomaly, Peter's Anomaly, Aniridia and Axenfeld's Anomaly.

  Symptoms may include hazy cornea, displaced or extra pupils and attachment of the iris to the cornea.

- **Trabeculectomy:** A surgical procedure to alleviate high intraocular pressure (IOP). A small part of the trabecular meshwork is removed to assist with the drainage of fluid.



- **Steroid Response:** Used to describe an incidence when a patient's intraocular pressure (IOP) has risen in direct response to a topical steroid being applied to the eye. Other steroids may also precipitate this response. The rise can cause glaucomatous damage to the eye if not treated.

- **Peripheral Iridotomy:** A small hole made by laser at the peripheral iris to allow fluid to drain into the anterior chamber. Usually performed for narrow/closed angles.

Would you like to know more?

If you have any questions regarding this research and how you can contribute, please feel free to contact the office at Flinders Medical Centre/Flinders University in Adelaide as follows:

Phone: +61 08 8404 2035 Fax: +61 08 8204 6722 Email: info@anzrag.com

*The **Australian and New Zealand Registry of Advanced Glaucoma** wishes to acknowledge and thank the organisations that support our work and research. Without their assistance this project would not be possible:*

◊Eye Foundation
◊Flinders University
◊Royal Society for the Blind
◊SA Pathology/IMVS
◊Flinders Medical Centre
◊Glaucoma Australia
◊The Ophthalmic Research Institute of Australia (ORIA)
◊ NHMRC Centre for Clinical Eye Research
◊Royal Australian and New Zealand College of Ophthalmologists (RANZCO)

Members of the Research Team:

Chief Investigator	Assoc/Prof Jamie Craig
Post Doc Research Fellow	Dr Kathryn Burdon
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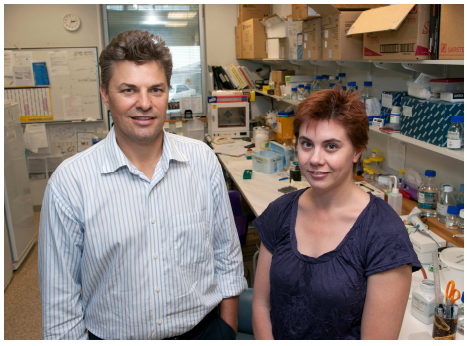
Coordinator	Bronwyn Usher-Ridge
Research Assistants	Kate Laurie & April Crawford
Technical Assistants	Abraham Kuot & Kathy Dowell



Assoc/Prof Jamie Craig and Dr Kathryn Burdon
Photo by: Ashton Claridge, Flinders University

Why am I receiving this newsletter?

Glaucoma is the name given to a group of eye diseases in which damage is done to the head of the optic nerve. In many cases the damage is created due to raised intraocular pressure (IOP) within the eye, which can be caused by poor drainage or blockage of fluid.

The risk of drainage problems may be higher in certain groups of people, such as those with pseudoexfoliation, pigment dispersion, closed or narrow angles and people whose anterior chamber (front part of the eye) has not developed normally. There is also a group of people who experience a sharp rise in IOP in response to the application of topical steroids.

The Australian and New Zealand Registry of Advanced Glaucoma has recruited over 2,500 samples from people with differing types of eye conditions. The aim of the registry has been to provide the world's largest cohort of advanced cases to further genetic research into the causes of glaucoma. Most of the people taking part in the registry have advanced glaucoma.

Other people taking part in the registry may have one of the subtypes of glaucoma, or may have an eye condition that predisposes them to a much higher risk of raised IOP and therefore to a much higher risk of glaucoma damage.

The registry is seeking to identify gene mutations that can cause these eye conditions to better understand them and to develop better screening techniques to identify those people at a high risk of experiencing glaucomatous damage.

Ophthalmologists across Australia and New Zealand have been recruiting people with and without glaucoma to help us in our search for disease-causing genes. The project needs a large number of samples from each group of eye conditions to allow the search to occur, and some of these conditions are not very common.

You may have provided a blood sample to the registry even if you have not been diagnosed with glaucoma as you may have a condition that puts you at risk of developing high IOP. You may also have provided a sample due to a family history of glaucoma as your ophthalmologist may think this indicates a genetic cause of the disease.

Recently we have begun recruiting samples from participants with definite glaucoma, but who have not reached the advanced stages. This is to compile a comparative group to the advanced cases. We are looking to find out if gene changes play a part in which people go on to develop advanced glaucoma despite treatment, compared to those who respond well to treatment and remain stable.

Some participants with advanced glaucoma and primary congenital glaucoma have been found to have gene mutations that have caused their glaucoma. We have invited other members of their families to be screened for these gene changes and they too are now part of the registry.

Helping ANZRAG to continue the fight against glaucoma blindness:

The work of this Registry is only made possible due to the funding provided by donors. Your important contribution, along with the funds raised by the Eye Foundation, will enable this groundbreaking work to continue. Please indicate below for information about financially contributing to the **Australian and New Zealand Registry of Advanced Glaucoma**. Please ask our staff to contact you to further discuss your donation or bequest options. *Mail to: ANZRAG, Dept Ophthalmology, Flinders Medical Centre, 1 Flinders Drive, Bedford Park SA 5042*

Name: _____

Please contact me by phone regarding a donation or bequest ☐ Ph: _____

Please contact me by post or email regarding a donation or bequest ☐ Address: _____

Thank you, but I am not in a position to donate at the moment ☐ _____