AUSTRALIAN & NEW ZEALAND
REGISTRY OF ADVANCED GLAUCOMA
Newsletter

Issue 4/ July 2014

Department of Ophthalmology
Flinders University
Adelaide, South Australia

Achievements:

The Australian and New Zealand Registry is very proud of the achievements we have made over the past 7 years. Not only has the project received a visit from a national figurehead (Dame Quentin Bryce, the former Governor General of Australia) we have also received exposure through print media, internet, television and radio.

Although the general public may hear about us in a radio or television interview or through a newspaper article, the professional community will more likely to be informed of our achievements through attending one of our national or international conference presentations or through publications in peer reviewed scientific journals.

This project has published a number of papers in peer reviewed journals by members of our research team.

Associate Professor Jamie Craig presenting for World Glaucoma Week 2014

Dr Mona Awadalla has been researching genes that may contribute to Angle Closure Glaucoma and a related eye condition named Nanophthalmos (small eyes). She has recently published a paper in the *JAMA Ophthalmology* journal titled *A mutation in TMEM98 in a large Caucasian Kindred with Autosomal Dominant Nanophthalmos linked to 17p12-q12.* You can read a summary of this paper in the following pages.

Emmanuelle Souzeau, our genetic counsellor, has published a number of papers. Her most recent publication titled *Predictive genetic testing experience for myocilin primary open-angle glaucoma using the Australian and New Zealand Registry of Advanced Glaucoma*, published in *Genetics in Medicine* this January, revealed the motivations of people, who have a family member diagnosed with a change in the *MYOC* gene, to be tested for the same mutation. We published some of her preliminary results last newsletter.

STOP PRESS

The ANZRAG team has just received notification that our latest paper has been accepted for publication in the prestigious journal *Nature Genetics*. In this extension of our previous work, we have identified three new open angle glaucoma susceptibility genes which are acting in our patients to increase their risk of vision loss. More details will follow in the next newsletter.

A mutation in TMEM98 in a large Caucasian Kindred with Autosomal Dominant Nanophthalmos linked to 17p12-q12

Nanophthalmos, a rare subtype of microphthalmia, is a developmental eye disorder affecting both eyes. It is characterised by the dimensions of the eye globe being significantly smaller than the normal range, causing serious complications such as severe hyperopia (farsightedness) and angle closure glaucoma.

Previous research has linked nanophthalmos to several specific genes and loci. Autosomal recessive (requiring two copies of the mutant gene to be inherited) disease has been linked to the gene *MFRP (Membrane frizzled-related protein)*. Another gene, also linked to autosomal recessive nanophthalmos, is *PRSS56 (Protease serine 56)*.

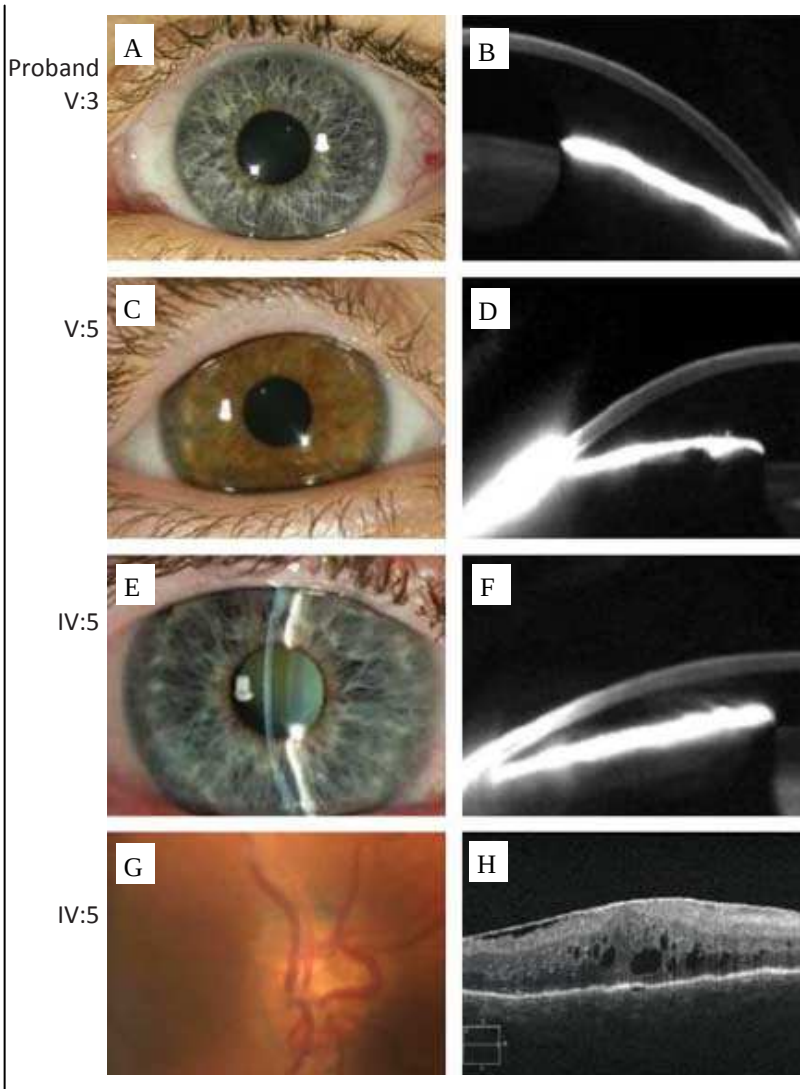
Our team, through the work of PhD candidate Dr Mona Awadalla at Flinders University, have recently reported findings in a large Caucasian family recruited into the Australian and New Zealand Registry of Advanced Glaucoma where many family members, located in Australia and England, had been diagnosed with nanophthalmos. The disease appeared to have an autosomal dominant mode of inheritance.

Linkage analysis detected a region on chromosome 17p12—q12 which overlapped a region previously reported in a Chinese family with nanophthalmos. Further analyses of 250 genes in the linkage region found only one novel variant had the potential to be the disease-causing mutation in this family. This variant caused the change of amino acid alanine to proline, the functional consequences of changing protein will be investigated in future research. This novel variant was shown to be present in all those with the disease and not present in those not affected.

Subsequently our colleagues in America have found more families affected with this very severe eye disease are explained by mutations in the *TMEM98* (*Trans-membrane protein 98)* gene.

There is little known about this gene, and further studies are warranted to understand how it causes nanophthalmos. This is the first study to report any gene causing dominant nanophthalmos.

Clinical Photos of the Affected Members in the Australian Branch of Family NNO-SA1



A, C, and E, External eye appearance of patients with nanophthalmos.
B, D, and F, Corresponding images obtained with a rotating Scheimpflug camera system (Pentacam; Oculus). Narrow iridocorneal angles and shallow anterior chamber depth were present in all affected eyes.
G, The optic disc with the presence of optic disc drusen.
H, Optical coherence tomographic image of the macula showing cystoid macular edema with epiretinal membrane.

How can my donation help?

The Australian and New Zealand Registry of Advanced Glaucoma largely operates on funds sourced from government funding and donations received through the Eye Foundation.

There are many costs associated with running the registry and the funding received is usually limited, and will need to be re-applied for every few years. The costs involved in keeping the registry alive include; administration costs, office consumable materials, replacing lost and damaged DNA collection kits, postage, laboratory consumable materials, wages, NATA accredited genetic testing, printing, and equipment.

The funds we receive from grants covers most of the costs, but will sometimes not cover everything.

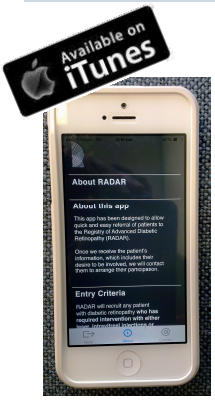
Your kind donations enable us to keep performing our research work and every cent is put to use in one of the areas listed.

Your tax deductible donation is banked with Flinders University in an account specifically set aside for this research. All of the funds received go towards the continuation of this vital project.

To date participants have kindly donated helpful funds to our project.

If you have any questions regarding making a donation or bequest please phone our staff on 08 8404 2035.

There's an App for that:



The Australian and New Zealand Registry of Advanced Glaucoma will soon have an App developed to assist in recruitment. The App will have a similar look to the one pictured and will be available on iOS and Android platforms.

Specialists will download the App for free from the iTunes store and Google Play and will refer patients to the project directly from their smartphone or tablet.

Once the referral has been received we will contact the new participant to arrange DNA samples. This process has been working well with a few selected specialists in another project as a trial.

Our team is proud to be at the forefront of utilising the latest in communication technology to ensure our research continues to remain successful and competitive.

A new initiative: The TARRGET program

Targeting At Risk Relatives of Glaucoma patients for Early diagnosis and Treatment

In a partnership with Glaucoma Australia and the Lions Eye Institute we are commencing a pilot study to increase knowledge and awareness of the increased risk of glaucoma to close family members of those known to be affected.

If people with glaucoma are diagnosed and treated early in the disease process, there is a much better chance that good vision can be maintained throughout life.

We already know that first degree relatives (children, siblings, and parents) of affected patients are more than 9 times more likely to develop the disease over their lifetime.

What the **TARRGET** program will do is examine, with new state of the art diagnostic approaches, what the pick-up rate will be amongst first degree relatives. We will start with a family member already meeting the criteria of ANZRAG for advanced field loss in a least one eye.

We will randomly select 100 cases of open angle glaucoma from ANZRAG, and then offer a free comprehensive glaucoma screening test for any of their first degree family members over the age of 40 (younger only in certain instances).

The idea is to include ***all*** close relatives, whether they have been seen or not before, and those who believe that they are not affected. This will provided a clear answer to how effective the new screening strategies could be if they were applied more widely.

These sort of studies can help us advocate for changes to Government policy to improve access and affordability for effective glaucoma screening strategies.

If you are selected for TARRGET, please try to encourage as many of your close family members as possible to participate.

Number Update:

GLAUCOMA TYPE	NUMBER
Angle Closure Glaucoma	408
Advanced Glaucoma	1738
Anterior Segment Dysgenesis	85
Glaucoma (Not Advanced)	661
Steroid Responders	153
Likely Myocilin (Not Advanced)	130
Nanophthalmos	43
Primary Congenital Glaucoma	107
Pigment Dispersion Syndrome	119
Pseudoexfoliation	520

We are continuing to recruit new participants steadily across all states and territories and across all types of glaucoma.

Our team have been working hard to recruit new participants steadily across all states and territories and across all types of glaucoma.

We now have 323 families where there are multiple members affected by the disease who have agreed to supply DNA samples to the registry. This will give us a much better chance of discovering new genes.

As the registry has grown we have begun recruiting more types of glaucoma to increase the depth of our findings.

Some glaucoma types are much rarer than others and each sample becomes very valuable to our study.

SOURCE	NUMBER
ACT	18
New Zealand	45
NSW	713
NT	32
QLD	52
SA	2060
TAS	369
VIC	391
WA	77

We are very grateful to all the specialists and participants who have, and continue to contribute to our success.

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:

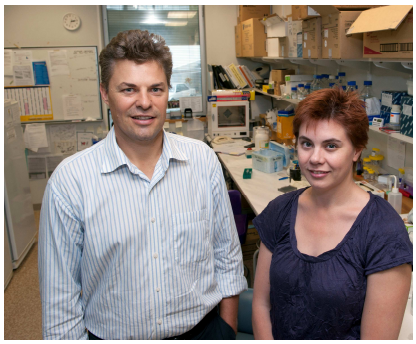
Phone: +61 08 8404 2035 Fax: +61 08 8204 6722 Email: info@anzrag.com

*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
- IMVS
- Flinders Medical Centre
- Glaucoma Australia
- The Ophthalmic Research Institute of Australia (ORIA)
- National Health and Medical Research Council
- Royal Australian and New Zealand College of Ophthalmologists (RANZCO)

Members of the Research Team:

Chief Investigator	Prof. Jamie Craig	
Post Doc Research Fellow	A/Prof Kathryn Burdon	
Genetic Counsellor	Emmanuelle Souzeau	
Coordinator	Bronwyn Ridge	
Research Assistants	Andrew Brown	Dr Tiger Zhou
	Dr Mona Awadalla	
	Lefta Leonardos	



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

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, has enabled this groundbreaking work to continue. Please indicate below if you would like 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. Cheques may be made payable to "Flinders University"

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: _____

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New Direction for Research: Register Your Interest

Skin biopsies to generate cell lines.

The Australian and New Zealand Registry of Advanced Glaucoma is looking to new directions in research to learn more about the disease and the possibility of new therapies. This exciting work will include creating stem cells from skin biopsies donated by participants already taking part in our study. We are keen to hear from you if you would consider providing a very small skin biopsy for our research.

This type of research will provide us with information regarding the molecular mechanisms involved in damage to the optic nerve head and, in the future, even creating new healthy tissue.

Small biopsies (4 mm) will be taken from the upper arm or inside the forearm under local anaesthetic.

Please consider donating to the skin biopsy project. You can register your willingness to participate by completing the form below and returning it in the pre paid envelope provided. Your name will go onto a list of potential donors who we will contact once we are ready to begin recruitment.

Name: _____ *Date of Birth* _____

Address: _____

Phone: _____

Email: _____

☐ *Please contact me by phone/email to further discuss this research*

☐ *Please add my name to the skin biopsy participation list*

Phone our office for more information on 08 8404 2035 or email info@anzrag.com