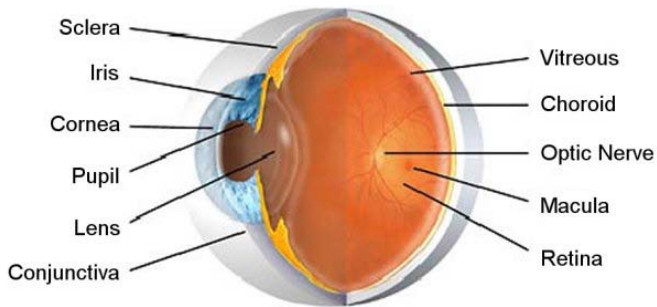


The Twins Eye Study

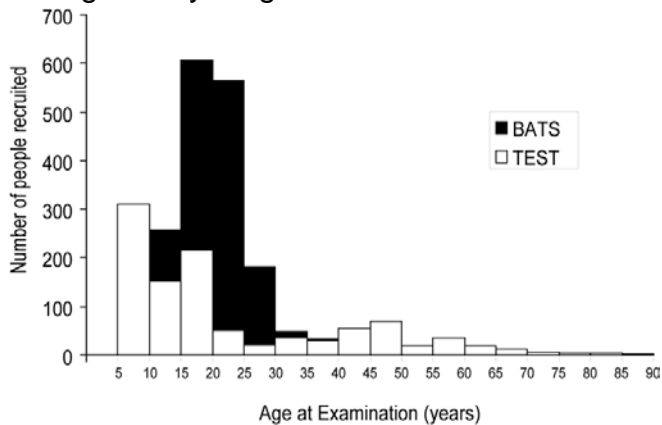
www.twinseyestudy.com

How good is your eye anatomy?

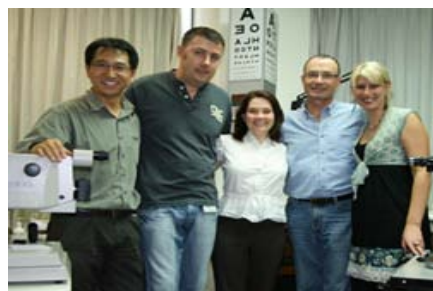


These are some of the parts of the eye that we are measuring in healthy people. We hope to discover genes that influence the measurements and find out whether these genes can lead to eye diseases like glaucoma and myopia (short-sightedness).

Since 2001 over 1,000 sets of twins and nearly 200 of their other brothers and sisters have been involved in the Twins Eye Study (TEST). (We examined some of the brothers and sisters to check that the twins had similar eye measurements to singletons and most of the time they do.) About half the twins were in Tasmania (TEST) and half in Brisbane (BATS) and a few from the other states and Norfolk Island. We saw all ages but most were teenagers or young adults.



(Ref Mackey et al *Twin Res Hum Genet.* 2009;12:441-54.)



Some of the Brisbane Twin Eye Team: Byoung-Sun, Bob, Colleen, David & Lisa

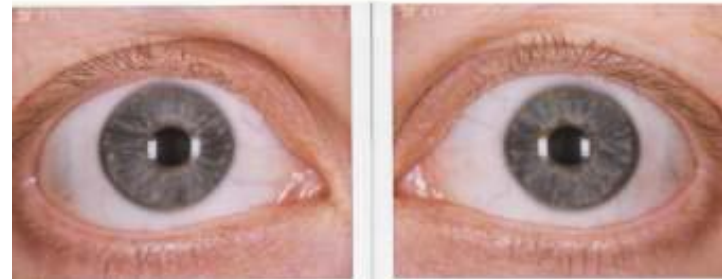
Some of the things we measured were:

- Visual acuity (how well you read the chart)
- Eye movements and 3D vision
- UV damage to the front of the eye
- Refraction (strength of glasses needed)
- Corneal thickness
- Axial length of the eye
- Intraocular pressure
- Optic nerve and vessels (using 3D photographs of the optic nerve).

Can you tell if twins are identical or not by looking at their eyes?



First set of twins above



Second set of twins below

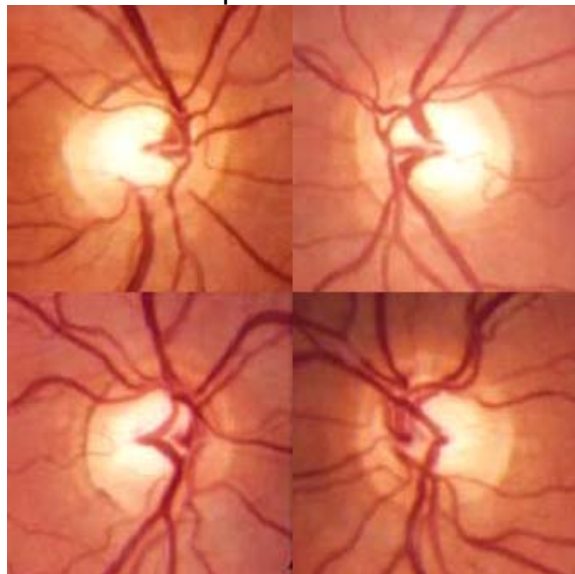


The 1st are identical and the 2nd are non identical.

We found out that by looking at the back of the eye, specialist eye doctors could correctly identify if twins were identical or not almost 90% of the time.

[\(Ref Hewitt et al Invest Ophthalmol Vis Sci. 2007;48:2469-75.\)](#)

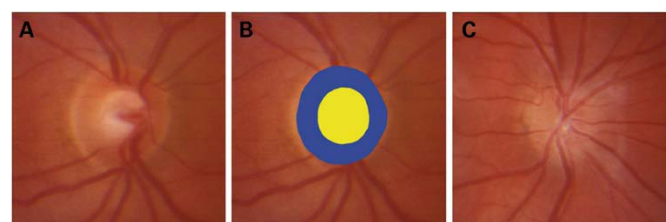
Photos of the optic nerves of identical twins



That tells us that genes are at work there!

Finding the genes for the size of the optic nerve!

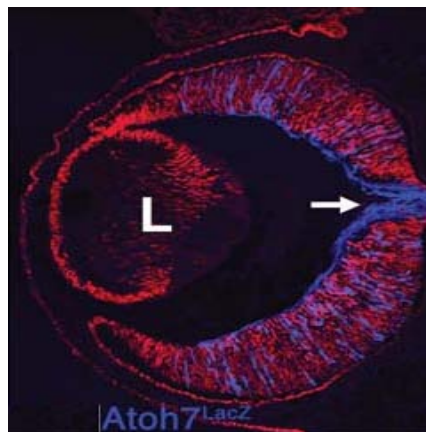
We measured the size of the optic nerves using a 3D computer to map out the edges.



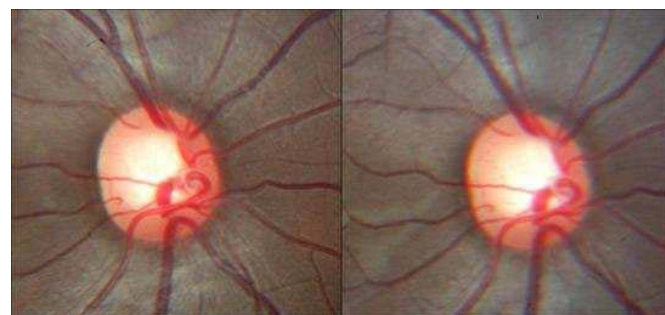
The optic cup is yellow and the optic rim is blue. The combined area is the disc size.

With these measurements performed on everyone in the TEST, we then compared over half a million DNA markers called SNPs and found one was frequently associated with larger optic nerve size. This was near a gene called *ATOH7*, which researchers had found was related to the optic nerve development in the mouse.

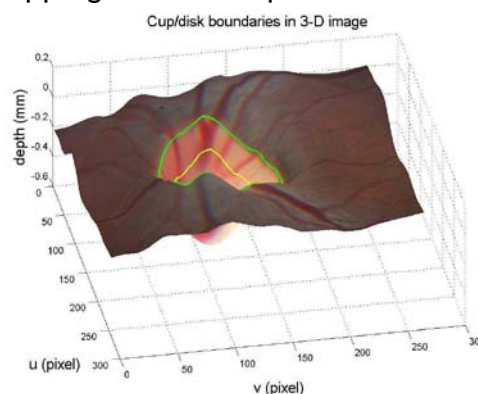
[\(Ref MacGregor et al Hum Mol Genet. 2010;19:2716-24.\)](#)



The blue shows where the *ATOH7* gene is expressed in the mouse eye – right in the middle of the optic nerve as we expected. These developing nerve fibres find their way back to the brain and transmit signals from the eye. Glaucoma is the most common disease affecting the optic nerve and we hope that this gene will help us understand more about glaucoma and other optic nerve diseases. There were some other genes that looked like they might affect the optic nerve but we need to study a lot more people to prove this. Often we find other research, like the UK Twins Eye Study led by Professor Chris Hammond, and by combining our data using a method called meta-analysis we are able to find more genes. The statistic experts at QIMR are among the best in the world for this.



Photos above converted to map below by 3D mapping of the disc photos

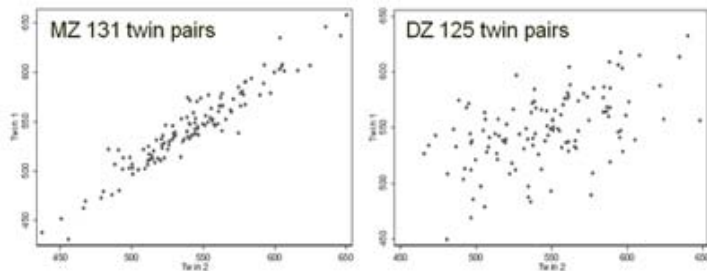


We have been working with some other American researchers who can turn our stereo photos into 3D maps of the eye.

[\(Ref Xu et al Opt Express. 2010;18:11347-59.\)](#)

[\(Ref Tang et al Invest Ophthalmol Vis Sci 2010;51:5870-7\)](#)

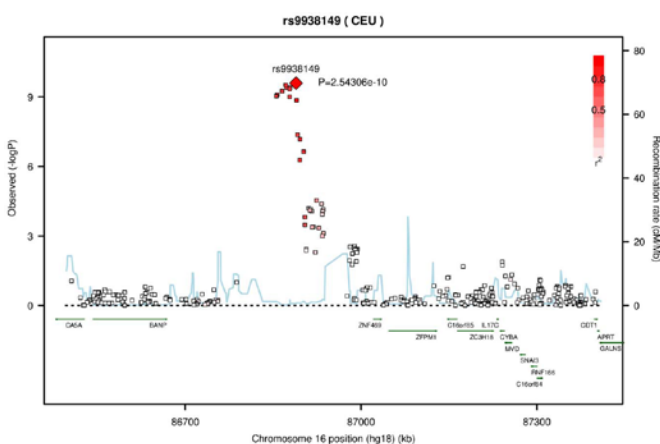
Finding the genes for the corneal thickness!



Early in the study we found that identical (MZ) twins (on the left) had more similar corneal thickness than the non-identical (DZ) twins (on the right). Indeed there was a 95% heritability so we were confident that we would find some genes affecting the thickness of the cornea, which is an important measure in glaucoma and for determining whether people are candidates for laser surgery for myopia.

[\(Ref Toh et al Invest Ophthalmol Vis Sci. 2005;46:3718-22.\)](#)

We did find some genes called *ZNF469* and *FOXO1*. The markers are shown on the graph below; when they rise above 7 (in dark red) we can be confident that they are really affecting the corneal measurement. There are still some more genes to find.



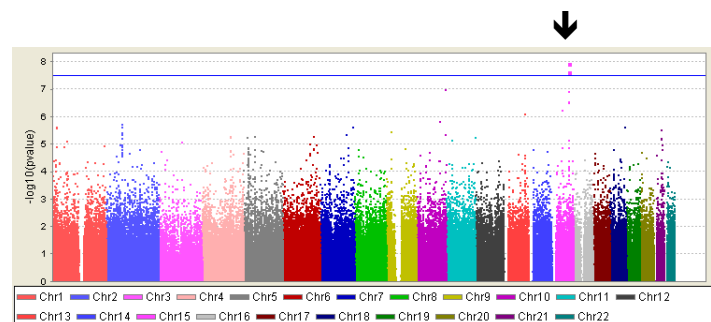
[\(Ref Lu et al. PLoS Genet. 2010;6:e1000947.\)](#)

Why do some people need glasses for distance?

We also found a gene region on chromosome 5 (the 5th largest chromosome) that is associated with the axial length of the eye. This is an important measure for the risk of becoming myopic.

[\(Ref Zhu et al Ophthalmol. 2008;115:1053-7.\)](#)

As part of an international collaboration with the TwinsUK research group led by Dr Chris Hammond at St Thomas' Hospital in London, we used a Genome Wide Association Study to identify genes associated with myopia.



The dots above the blue line indicate the *RASGRF1* gene, which contributes to myopia in older twins. This was also found in a large group of Dutch twins and population studies of myopia.

[\(Ref Hysi et al Nat Genet. 2010;42:902-5.\)](#)

The Dutch group also identified another gene associated with myopia *GJD2*, which was replicated in the older UK Twins.

[\(Ref Solouki et al Nat Genet. 2010;42:897-901.\)](#)

We are now working with several international and local groups to identify genes associated with myopia in younger individuals.

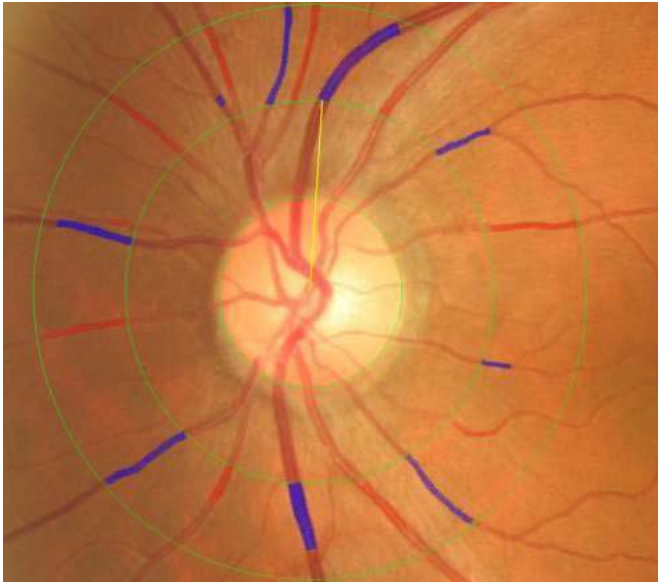
New Gene for Glaucoma

In our other major project: The Glaucoma Inheritance Study in Tasmania (GIST), as part of an international consortium led by deCODE Genetics in Iceland, we helped identify the gene *Caveolin* as being associated with glaucoma.

We tested for association of *Caveolin* with intraocular pressure, central corneal thickness, hypertension, type 2 diabetes and myopia in Twins Eye Study and of the traits tested, a mild association was only observed for increased intraocular pressure.

[\(Ref Thorleifsson et al Nat Genet. 2010;42:906-9.\)](#)

Studies of Retinal Blood vessels

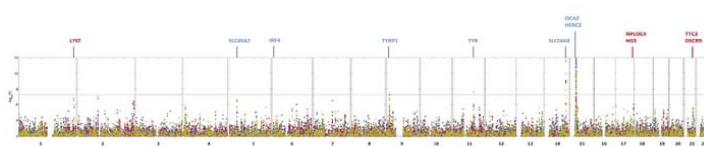


In conjunction with the UK twins study, we found the relationship between the calibre of retinal arteries and veins is genetically mediated and each is associated with risk of cardiovascular disease.

([Ref Fahey et al Invest Ophthalmol Vis Sci. 2010 Oct 6](#))

More Genes for Eye Colour

Several years ago the BATS played an important role in the identification of the OCA2 gene in eye colour. A recent collaborative study between Dutch, UK and Australian twins identified several new genes for eye colour.

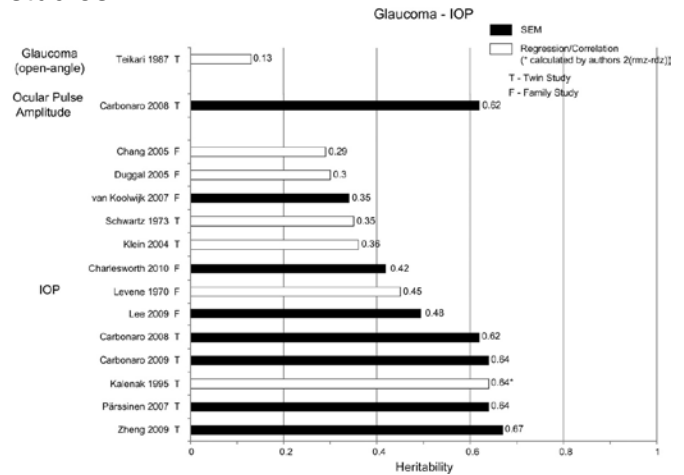


([Ref Liu et al PLoS Genet. 2010 May 6;6:e1000934.](#))

Review of previously published twin & family studies shows many eye measurements are heritable

Heritability is the proportion of variation in a population that is attributable to genetic variation. Many ophthalmic disorders and biometric traits are known to have a genetic basis. A total of 82 articles were retrieved from the literature relating to estimation of heritability for an ocular disease or biometric trait; of these, 37 papers were concerned with glaucoma, 28 with refraction, 4 with acute macular degeneration, 5 with diabetic retinopathy, and 4 with cataract.

Twin studies of intraocular pressure show higher heritability estimates than family studies.



([Ref Sanfilippo et al Surv Ophthalmol. 2010;55:561-83.](#))

Is everything genetic?

We are also looking at environmental factors that influence the eye.

In the Tasmanian Twins, we found that if the mother smoked during pregnancy then there was an increased risk that the twins would have a turn in their eye (strabismus) and poor 3D vision (10% of people have poor 3D/stereo vision and therefore don't get the full effect of 3D movies like Avatar.)

([Ref Ponsonby et al. Ophthalmic Epidemiol. 2007;14:351-9.](#))

We also found that smaller birth size was associated with narrower blood vessels in the eye.

([Ref Sun et al Hypertension. 2009;54:788-95.](#))

Lower birth weight was associated with shorter axial length and more curved corneas. Although both these measures are associated with myopia, birth weight was not associated with myopia. This adds new insights into the mechanism for myopia.

([Ref Sun et al Am J Ophthalmol. 2010;150:909-16](#))

MISSED THE EYE STUDY AND WANT TO BE A PART?

Professor David Mackey and his team will be making a few weekend visits to Brisbane in mid 2011. If you would be interested in participating in the 2-hour eye exam please let us know D.Mackey@utas.edu.au and we can confirm the dates. Anyone living in Perth, Melbourne or Tasmania can also be seen in those locations. If you know your twin missed out, there is an opportunity now for a thorough eye examination.

DO THE MEASUREMENTS CHANGE AS WE GET OLDER AND WHAT INFLUENCES THESE CHANGES?

We hope to do a 10-year follow-up of the Twins Eye Study in Tasmania and Brisbane starting in 2013. So please keep in touch.

If you have any questions relating to your eye exam with us, or your own eye care provider would like a copy of the photos or measurements, please let us know or contact Professor Mackey on the email above.

You can log on to the eye study web site and the links there will take you to the journal articles if you would like to read them.

THANKS AGAIN FOR PARTICIPATING IN THE TWINS EYE STUDY (TEST)

OUR COLLABORATING CENTRES

Australian Twin Registry

www.twins.org.au



Centre for Eye Research Australia

www.cera.org.au



Centre for Eye Research Australia

Lions Eye Institute

www.lei.org.au



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Queensland Institute of
Medical Research

Twins UK, St Thomas' Hospital, Kings College

www.twinsuk.ac.uk



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