The Genetic Basis of Glaucoma
Part Three of Three

This is the final in a series of three articles written for our readers by Dr Andrea Vincent, recipient of a research grant from Glaucoma NZ in 2007.

New Zealand Research In Glaucoma Genetics.

The current knowledge for the genetic basis for glaucoma is being slowly elicited in research laboratories around the world. Since the first gene known to cause glaucoma, Myocilin, was characterised in 1995, further research has elucidated the nature of 3 other genes, Optineurin, WDR36 and CYP1B1, with evidence that at least 8 other genes exist.

With the assistance of funding from a Glaucoma NZ research grant, we are attempting to characterise the genetic nature of glaucoma in New Zealand. Overseas research centres have been involved for years, with vast libraries of DNA (and lots of money!), but it is still worthwhile to carry out such research in New Zealand.

Firstly we have identified a number of affected individuals with a positive family history of glaucoma, i.e. at least one first degree relative affected. After informed consent we take a blood sample, a cheek swab, or a saliva specimen for DNA extraction.

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Our screening strategy is firstly to sequence the Myocilin gene. The frequency of Myocilin mutations is about 4% in the populations already characterised, so in a group of 100 patients we would expect to only find 3 or 4 with a disease-causing sequence change, or mutation. In those with a mutation, we then recruit their family members, both affected and unaffected, to make sure the mutation occurred only in conjunction with the disease, and not in the unaffected individuals.

As Myocilin is very well characterised we could then check with databases and research publications to ascertain whether our mutations have been characterised before. Our research can add to the pool of knowledge helping to confirm the status of a sequence change, or maybe even finding new mutations.

After screening the Myocilin gene, we would then screen OPTN, WRD36 and CYP1B1. It is likely after this process that at least 85-90% of patients would not have a genetic diagnosis, and it is this group of patients and their families which provide us with a powerful tool to identify new genes. Certainly when a very large, multiple generational family is discovered, with no mutations identified in known genes, a genetic method known as Linkage, can be employed to try and determine if the disease “links” to a certain area of a chromosome. Then we would look for genes within that area of a chromosome.

Although this work is very time-consuming and expensive, screening a New Zealand Glaucoma population for genetic causes can contribute to the world-wide knowledge, and has the potential to identify new genes.