

[www.eye.usyd.edu.au/research/macular.html](http://www.eye.usyd.edu.au/research/macular.html)

*Our aim is to develop new treatments that reduce blindness from macular disease, through multidisciplinary, patient oriented, world class research*



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## The Macular Research Group

Welcome to the 2<sup>nd</sup> edition of Macular News!

In the last newsletter we described the stem cell research activities of the lab research unit. In this issue we will tell you about our clinical research activities. The Macular Research Group of Sydney University's Save Sight Institute has three units: the "Fight Retinal Blindness!" national audit of response to treatment of wet macular degeneration, a laboratory research unit and a clinical research unit. The clinical research unit conducts our own "investigator-initiated" studies as well as those that are sponsored by drug companies.

## The Clinical Research Unit

undertakes trials and studies involving research into the treatment and mechanisms of age-related macular degeneration, diabetic retinopathy, central and branch retinal vein occlusion and macular telangiectasia. Since 1998 we have conducted four major clinical trials, each lasting 3 – 5 years, that have been hailed internationally as major advances in the treatment of macular disease.

## Clinical Research

We have a long history of conducting our own major "randomised clinical trials" (RCTs). In RCTs, patients with the condition being tested are randomly allocated (like the toss of a coin) to receive the standard or the new treatment. One important principle of RCTs is that the person measuring the outcomes (e.g. letters read on a chart) is "masked" i.e. doesn't know what treatment the trial participant they are testing is getting. If they knew they were getting the drug being tested, they might be tempted to push the patient to read more letters than they otherwise would have, because everyone wants the test drug to work. RCTs take an enormous amount of time and resources to plan and conduct to a high standard, but they are always worth doing because they are the most rigorous test of whether a drug works or not for a particular disease. Positive results from RCTs are usually required these days before a drug or "intervention" can be used routinely in the clinic.

## The team



*From left: Dr. Meidong Zhu, Martin Lee, Haipha Ali, Prof. Mark Gillies, Pari Herrera-Bond, A/Prof. Samantha Fraser-Bell, Ann Gould, Mila Kolmogorova*

*Absent: Amy Kenyon, Dr Christine Gaston, Dr Alex P Hunyor, Maria Williams*

**In this issue we introduce you to our cutting edge CLINICAL RESEARCH and give you the opportunity to support it**

## Investigator Initiated Studies

The clinical trials that we have conducted have mostly tested steroid injections into the eye to treat macular disease. In fact, researchers at the Save Sight Institute and Sydney Eye Hospital were the first in the world to begin injecting steroids for the treatment of retinal disease in the early 1990s. Many, but not all, of these trials have been supported by Australia's peak body for funding medical research, the National Health and Medical Research Council. Our first major trial (1998-2002) tested an injection into the eye of triamcinolone, a slow-release steroid, for wet macular degeneration. We were disappointed not to find a beneficial effect, however this information was still extremely influential worldwide on the treatment of macular degeneration since it discouraged the use of triamcinolone and stimulated the search for better treatments.

Our next major trial was the Triamcinolone for Diabetic Macular Oedema study (2003-2005). This trial, which was extended for 5 years, was the first in the world to prove beyond doubt that steroids could be highly effective in restoring vision in eyes with swelling of the macula which had not responded to conventional (laser) treatment. Swelling, or "oedema", of the macula is the commonest way for people with diabetes to lose vision.

## Investigator Initiated Studies

After proving that steroids could work, we undertook another major RCT (2006-2008) as the lead centre with 3 other centres in Australia to see whether steroid treatment could be combined with laser for the best outcomes in our patients. In fact the two treatments did work better than laser alone when used in combination, but the trial emphasised that the treatment could take up to two years to work. Throughout all these studies we have carefully monitored and reported the side effects of steroid injections into the eye, which includes a significant risk of cataract (cloudy lens) and elevated intraocular pressure, which can cause glaucoma if not treated. These side effects are manageable, but this requires patients to be followed carefully.

A study we have just commenced, also as the lead centre, will compare steroids with the other type of drug that has now been shown to be effective for macular oedema, Vascular Endothelial Growth Factor (VEGF) inhibitors. VEGF inhibitors, which have revolutionised the treatment of wet macular degeneration, have also recently been shown to be effective for macular oedema. They do not seem to cause cataract or elevation of the intraocular pressure, however they are not as strong as steroids and must be injected more frequently, i.e. 4-6 weekly compared with 4-6 monthly for steroids. We have been able to secure a supply of "Ozurdex" a new slow release steroid developed specifically for the eye that seems to have fewer side effects than triamcinolone. We are comparing Ozurdex head-to-head with Avastin in the first such study of these new treatments ever conducted.

## Sponsored Studies

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The Clinical Research Unit of the Macular Research group is regularly included as a centre in major international clinical trials of drugs and interventions for macular disease that have been developed by drug companies. Over the last 8 years we have conducted more than 30 studies into a range of macular diseases, such as wet and dry macular degeneration, diabetic retinopathy and retinal vein occlusion. While some studies have not been successful, others have been spectacularly so, for example the study of ranibizumab (Lucentis) for wet macular degeneration in which several of our patients could access this remarkable treatment before it became freely available for clinical use a few years later.

## Our Staff

Clinical trials need many people to run them properly. For every study there is an injector (if the drug is injected into the eye as it often is these days), a masked and unmasked coordinator and at least 2 masked observers, each of which needs to have a backup. Sometimes people from up to 6 studies are seen in the same research clinic. We have six part-time coordinators: We have six part-time clinical coordinators, a retinal photographer, 1 administrative assistant and 4 Ophthalmologists (eye doctors), including a retinal fellow (advanced trainee) from the Retina Unit of the Sydney Eye Hospital.

One of the strengths of our clinical research unit is its close association with our laboratory research unit on one hand, and on the other New South Wales' leading tertiary referral centre for eye disease, the Sydney Eye hospital. Such an arrangement facilitates "bench to bedside" or "translational" research, in which discoveries in the lab can be developed as new treatments in the clinic. Triamcinolone was a shining example of this process.

## Support our research

In contrast to laboratory research, which often needs money for equipment and lab supplies, the main expense in clinical research is personnel. While we do get remunerated for participating in sponsored studies, the sponsors are so particular about the patients they will accept into the study that sometimes we only enrol 2 or 3 patients. At the moment everyone in the Unit is often working significant overtime just to keep up. Support for the clinical research unit will allow us to engage an extra clinical research officer to collate, manage, process and check data from our own investigator initiated studies. This will allow other coordinators to focus on what they do best, assisting patients.

The entire research group relies exclusively on external grants and fundraising. We receive funding from sources such as:

- National Health and Medical Research Council (NH&MRC);
- Royal Australian & New Zealand College of Ophthalmologists – Eye Foundation; and
- Lowy Medical Research Institute.

To make a donation to support the clinical research team at the Save Sight Institute and the Sydney Eye Hospital, you may send a cheque to Professor Gillies made out to the "Macular Research Group" at the address below. No amount is too small or too large. Any excess funds will be used to establish a scholarship for future PhD students, of which we start around one every year.

Alternatively you may complete the enclosed donation form.

*You have received this newsletter because you have, or you have shown interest in, macular disease. If you do not want to receive this newsletter, just let us know on 02 9382 7309.*

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## Where are we located?

You will find us at the Save Sight Institute, located at: □  
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