



**NATIONAL
EYE
RESEARCH
CENTRE**
YOUR SIGHT
OUR VISION

NEWSLETTER

Spring • 2011

PATRON'S VISIT TO BRISTOL AND LEEDS

HRH Prince Michael of Kent, Patron of the **National Eye Research Centre**, visited both Bristol and Leeds during 2010 to be briefed on current research, achievements and future plans. As well as viewing poster displays depicting research projects, His Royal Highness had the opportunity to meet research staff and some of the charity's supporters and in Bristol his visit initiated the celebration of the bicentenary of the Bristol Eye Hospital.



Colonel Sam Gausson bids farewell to Prince Michael of Kent

BENEFITS OF NEW CLINICAL RESEARCH UNIT IN REFURBISHED BRISTOL EYE HOSPITAL

During its bicentenary year the refurbishment of the Bristol Eye Hospital started and the new facilities will greatly benefit patients and staff. An important new facility is a greatly expanded Clinical Research Unit which will significantly benefit the culmination of eye research projects and patient eye care.

GREAT RESEARCH PROVIDES GREAT CARE

THE DIRECTOR OF RESEARCH, PROFESSOR ANDREW DICK WRITES

This year Bristol Eye Hospital opens a new clinical research facility. Not only does this emphasise the value and raise the importance of research but with its location in the hospital directly at the hub of clinical service delivery, makes sure that patients are at the heart of all future developments and success.

The hospital within University Hospitals Bristol NHS Foundation Trust has made considerable investment with grants from Above and Beyond Charity, National Eye Research Centre and pharmaceutical support into infrastructural refurbishments throughout the hospital. Alongside the structural developments, the

University and Trust partnership works to provide research as core business with the clear and tangible result of improved patient outcomes and care.

The refurbished Clinical Research Unit (CRU) presents us with a platform to enable engagement of University activities and the charities investment over the years and an ability to move more timely our results from the laboratory to generate new treatments as well as the reverse; taking patient data and samples to the laboratory to help find why it happens and how we can find better therapies. One major programme of our work is toward



Prince Michael of Kent discussing posters with Professor Andrew Dick

identifying the causes, tests to diagnose and development of therapeutic targets for inflammatory, angiogenic (like diabetic retinopathy and age-related macular degeneration) and degenerative disorders of the retina.

The work is only possible because of the partnerships within the programme between NERC, industry, university and the NHS. As I have said previously: "charities like NERC support the discovery and development that makes real differences to our patients, but only when the UK researchers work collaboratively within teams of University Researchers, NHS consultants and our industry colleagues".

Now with the CRU our mission can expand. Currently our work on identifying the role of Tumour Necrosis Factor (TNF) in ocular inflammatory disease (uveitis*) has informed and led to improved care; we are currently leading both our own trial (funded by National Institute of Health Research and Arthritis Research UK, ARUK) and via industry (Abbott) on randomized controlled trial of anti-TNF therapy in the treatment of uveitis in children and adults, respectively. Currently our Clinical Research Unit is undertaking over 20 randomised clinical trials, some sponsored by the pharmaceutical industry, other trials and studies, known as 'investigator driven' are funded via charity. Additionally the clinical research unit runs studies that allow us to interrogate the impact of disease and therapies on quality of life and health economics as well as the science of identifying the cause and tests that may help us diagnose as well as designing tests to identify those patients at most risk and those that may respond to therapy.

So finally, with our intrinsic determination, we are now achieving the wish that all patients will have an opportunity to benefit directly from research, giving choice of treatment when they come to hospital as well as contributing to research for future benefit. In addition to the CRU staff, the CRU has brought together NHS staff and the laboratory scientists to engage to make this happen.

*For more information on uveitis; see Uveitis Information Group. <http://www.uveitis.net/uig/index.php>

INFLAMMATORY EYE DISEASE RESEARCH

BY DR LINDSAY NICHOLSON

Work on inflammatory ocular research in the University of Bristol laboratories in 2010 advanced our understanding of both basic immunological mechanisms underlying inflammatory eye disease and novel therapeutic approaches with the potential to develop into treatments for disease. We know that uveitis is caused by cells of the immune system which attack the normal tissues of the eye and prevent them working properly. A normal eye does not contain activated immune cells, and one key to treating these diseases is developing a clearer understanding of the mechanisms that bring these white blood cells into the eye. We believe that this happens because molecular signals appear both in the eye and on immune cells that draw them from the blood into the tissue. Drugs that target these molecular signals can be used to modify the passage of cells into the eye, so it is important to understand which cells we want to exclude and which we might want to encourage. Using equipment that was purchased with the help of NERC, we have completed an extensive analysis to identify the types of cell that are involved. We now understand in more detail how the mixture of different cells changes as the disease progresses. This is important because some of these cells may play a role in making disease worse, but other types regulate the damaging inflammation.

Perhaps if the healing cells can be encouraged they can carry out their function more effectively. In the future we hope to raise further funding to test whether this is the case.

Other work which is much closer to the clinic takes a similar approach but uses a less specific inhibitor of cell trafficking called fingolimod. In 2008 we published a study of this drug that suggested that it might be very effective in halting ongoing eye inflammation. Since this work was published we have continued to develop this approach in collaboration with industrial partners. Because fingolimod is already licensed for the treatment of patients with multiple sclerosis, if it does prove to be effective in uveitis, it can be applied in the clinic in a much shorter period of time than more experimental therapies, since it will not have to cross as many regulatory hurdles. We believe the combination of basic research that focuses on understanding the detail of immune cell trafficking into the eye, in combination with studies of the best drugs available at present for interfering with this process, within the same research group, will drive progress to more selective treatments that will have fewer side effects. This line of approach will continue to be a focus of the research group in succeeding years.

IMPROVING CORNEAL TRANSPLANT SURVIVAL

BY PROFESSOR JOHN ARMITAGE



Prince Michael of Kent meeting Professor John Armitage and Miss Clare Bailey

Corneal transplantation is one of the oldest transplant operations, dating back more than 100 years. Many transplants are very successful at restoring vision but, despite significant advances over the years such as the introduction of antibiotics, operating microscopes, and improved surgical instruments and technique, there are certain groups of patients where the risk of failure remains high. The main reason for graft failure in these patients is immunological rejection where the corneal transplant recipient's own immune system recognizes the graft as 'foreign' and attacks it. Organ transplants are especially vulnerable to rejection and tissue matching, similar to blood group matching but based on white rather than red blood cells, reduces the risk of rejection. In this issue of the NERC Newsletter, Dr Sue Nicholls gives an overview of her laboratory research into corneal transplant rejection. Sue's research has certainly increased our understanding of the corneal transplant rejection process

and opened up new avenues for investigation. In tandem with Sue's work, we have been running a clinical trial for the past 10 years to investigate the impact of tissue matching in patients whose corneal transplants are at increased risk of rejection ('at risk' grafts). This Corneal Transplant Follow-up Study II (CTFS II) initially received start-up funding from the Department of Health for three years and has since been supported by the National Eye Research Centre. This is a prospective, multi-centre study involving surgeons in more than 30 hospitals around the country. Unlike previous studies, all of the tissue-typing of eye donors and corneal transplant recipients uses DNA techniques to ensure the accuracy of typing and matching. We are nearing the target of 1200 matched corneal transplants in this unique investigation worldwide, but we still have to wait a further five years to gather all of the required clinical follow-up data on the occurrence of graft rejection. However, interim analyses have already produced some exciting preliminary results, such as the impact of age on the risk of graft rejection. It appears that at risk corneal transplants in older patients are less likely to suffer rejection than at risk grafts in younger patients, a finding that has been hinted at in previous studies but now has been given a firmer support. It is a long time to wait for the final analysis of the data, but CTFS II should deliver some definitive answers that will not only provide guidance to ophthalmic surgeons on the best options for their patients but will also inform laboratory studies, such as those of Dr Nicholls, aimed at improving our overall understanding of the immunology of the rejection process. This is a key strength of eye research in Bristol where we are able to run parallel laboratory and clinical studies, supported by funding from NERC.

CORNEAL GRAFT REJECTION

BY DR SUE NICHOLLS – WHO HAS BEEN SUPPORTED AS A RESEARCH FELLOW BY THE CENTRE SINCE 1987

Dr Sue Nicholls joined the Department of Ophthalmology in 1987, soon after NERC was established under the leadership of Professor David Easty. She gained her PhD with Dr. Terry Hill, studying immunity to herpes simplex, the cold sore virus, in the Department of Microbiology (now the Department of Cellular and Molecular Medicine). Herpes simplex infection of the cornea can cause scarring and blindness, only curable by a corneal transplant. Thus it was a relatively seamless transition when she moved to Ophthalmology to study corneal graft rejection. In collaboration with Professor Ben Bradley, then Director of the UK Transplant Service, and David Easty, she examined the effect of different types of tissue matching

(known scientifically as "histocompatibility matching") on corneal graft rejection. In other areas of transplantation, such as kidney or bone marrow, matching between donor and recipient at genes of the so-called "major histocompatibility complex", were known to be the most important for determining success of the transplant. Sue was therefore surprised to find that matching of a different group of genes, known collectively as "minor histocompatibility genes", was equally, if not more, important in determining the success of a corneal graft. These important experimental findings were published in 1991 (Nicholls et al., Invest. Ophthalmol. Vis. Sci.) and were later confirmed and followed up by groups in the USA

and elsewhere. Our experimental work on tissue matching continues alongside the long-term clinical "Corneal Transplant Follow-up Study", led in Bristol by Professor John Armitage.

In collaboration with Dr. Carolyn Shimeld, also a herpes simplex expert, Sue refined techniques for visualising cells of the immune system in thin slices of tissue (Whiteland et al., J. Histochem. Cytochem 1995) and has provided advice on the technique to numerous laboratories working in different areas of immunology, both in this country and abroad. She has continued to use such expertise to examine the immune response within the cornea, in both corneal graft rejection and herpes simplex virus disease. Herpes simplex virus infection can recur in the cornea, rather like a cold sore on the skin, and cause graft failure. In studying this recurrence, she identified the granulocyte as the major immune system cell controlling the spread and elimination of the virus. In mapping the distribution of recurrent virus in the cornea she further identified the graft-host junction as the major location of virus spread (Nicholls et al., Invest. Ophthalmol Vis. Sci., 1996). These findings have had implications for treatment of both herpes simplex infection and corneal graft rejection.

The investigation of communication between cells of the immune system is part of on-going research and crucial for highlighting potential therapies. Many "messenger" molecules exist and Sue has recently concentrated on three of them: interferon gamma, nitric oxide and a cell surface molecule, CD200 that inhibits macrophage activation (Nicholls and Dick, Invest. Ophthalmol Vis. Sci., 2008).

Recent collaboration with Professor Mick Bailey in the School

of Clinical Veterinary Science has resulted in development of a "pre-clinical" model for testing future therapeutic agents and is providing the opportunity to train veterinary students in basic ocular research, ophthalmology being an increasingly important veterinary speciality. This collaboration, together with clinical observations of the growth of blood vessels in the cornea, has led us to a new avenue of research into how undesirable blood vessel growth can be controlled. Such research is relevant not only to corneal graft rejection, but to other diseases where blood vessel growth has pathological consequences, such as in retinal disease or cancer.

None of our corneal graft rejection research would have been possible without the contributions of clinicians, technicians and students and the generosity of NERC and its donors. A major role of research scientists in the department is to train clinicians in basic research. Three clinicians deserve special mention, who, as research fellows, were supervised by Sue and made substantial contributions to the research; Francisco Figueiredo, (PhD, 1996), now a consultant ophthalmologist at Newcastle where he continues his own corneal research, Chun-Ho-Lau (MD, 1998), who now runs his own research laboratory in China, and Sanjiv Banerjee (PhD, 2006), now a consultant ophthalmologist in Cardiff. In addition to funding from NERC, support has also been provided by the RNIB, Guide Dogs for the Blind Association, Wellcome Trust and Medical Research Council.

For more information about corneal graft rejection visit:
<http://www.bristol.ac.uk/clinicalsciencesouth/ophthalmology/research/grfts/>



(Part of the National Eye Research Centre) Reg. Charity No. 294087

YORKSHIRE EYE RESEARCH

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Appeal Administrator: Ms Susannah Voke

In the past year, our funding of three projects has brought significant advances in the scientific understanding of the detection of retinopathy in prematurity, prevention of glaucoma, cataract and diabetic retinopathy and the treatment of retinoblastoma; an eye cancer affecting children and infants. Dr Carmel Toomes has successfully identified another inherited gene which makes premature babies susceptible to severe sight

loss; this work will result in the development of DNA swab post natal diagnostic test leading to early sight saving intervention. Mr Andy Cassels Brown, Consultant Ophthalmologist and his Public Eye Health "Save Your Sight" team have won the 2010 Allergan Glaucoma Award for outstanding contribution to eye health in Yorkshire. The Save Your Sight campaign focuses on removing barriers to eye care such as social exclusion and poverty by going out into the community and working with individuals in receipt of glaucoma, cataract and diabetic retinopathy. All three of these conditions are treatable if diagnosed soon enough. The Team now has a mobile unit and the campaign is to be extended across the north of England. We are also delighted to be able to report that Dr Ian Simmons' retinoblastoma pilot at the University of York and with colleagues and patients in Uganda has been a resounding success; all children within the treatment programme are alive and in remission.

Currently we are continuing to seek funds to support Dr Manir Ali's project to find the genetic causes of Primary Open Angle Glaucoma which affects 1 in 50 adults in the UK and although treatable in its early stages, it remains extremely difficult to diagnosis as physical irreversible symptoms only occur late in its prognosis. Knowledge of the genetic causes would allow the

Continued on back page...

PLEASE GIVE GENEROUSLY TO HELP SAVE SIGHT

YES, I would like to support the National Eye Research Centre in the following way.

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Postcode: _____

Here is my gift of: (please tick)

£1,000 £500 £250

£100 £50 £25

Other £ _____

Or debit my Access/Visa/CAF Charity Card

Account Number:

Expiry Date _____ / _____

I want the charity to treat all donations I have made since 6 April 2000 and all donations I make from the date of this declaration until I notify you otherwise as Gift Aid donations.

Signature: _____

Date: _____

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The National Eye Research Centre

I would like further details about: (please tick)

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Please detach and return your completed form to:

The Appeal Director,
National Eye Research Centre,
FREEPOST, Bristol Eye Hospital,
Bristol BS1 2BR

Tel: 0117 9290024 Registered Charity No. 294087

FUNDRAISING NEWS

Every year we rely heavily on the generosity of our supporters to continue current research programmes and keep the research laboratories at a high standard to develop new cures and treatments.



Thanks to our supporters we have continued to fund research - including provision of the latest equipment in Bristol, Leeds and other eye centres countrywide. In these difficult financial times where universities have had their government funding for research reduced, it is essential that the Centre maintains its backing of the research laboratories as well as funding research projects.

The visits of **HRH Prince Michael of Kent** to Bristol and Leeds greatly encouraged the researchers who presented posters depicting their research and enlightened supporters. His Royal Highness's interest is greatly appreciated.

The summer **Garden Party** held at Cotswold Farm, near Cirencester was greatly enjoyed and additional useful funds were raised through support of a musical evening at the Bristol Hippodrome where supporters enjoyed a performance of "**The Sound of Music**" preceded by supper at the **Bristol Royal Marriott Hotel**.

We are so grateful to the many charitable trusts and businesses who support us as well as so many individual donors, whose donations are boosted by **Gift Aid**, where appropriate. Those who give regular support by **Standing Order, Direct Debit** or **Payroll Giving** are particularly appreciated, as are those who organise fundraising activities, be it a coffee morning, plant sale or sale of Christmas cards. Once again the **Owls of Pill** contributed generously following their successful carol singing in December.

There is still much to be discovered to reduce sight loss and improve the quality of life. Our supporters' generosity really does help.

We urge our supporters to join those who are competing in the Great Weather Lottery and regularly winning prizes.

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JOIN OUR SUPPORTERS WHO ARE REGULARLY WINNING PRIZES IN THE GREAT WEATHER LOTTERY

WIN £10,000 DAILY
with the **NATIONAL EYE RESEARCH CENTRE**

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- For just 20p a day you can win up to £10,000
- 31.5% of the funds come back to the National Eye Research Centre, even after all the prize payouts
- Prizes are posted to your door
- You can pay by standing order or cheque
- The top prizes are insured at Lloyds of London

YORKSHIRE EYE RESEARCH (continued)

development of an accurate DNA swab test and therefore method of screening for the disease. We also continue to support Prof. Chris Inglehearn's ongoing project to determine the causes of inherited retinitis pigmentosa, cone-rod dystrophy and microcornea in the hope of developing gene therapies for these blinding childhood diseases. Professor Inglehearn's research in 2009 identified mutations of the ADAM9 gene as the cause inherited cone-rod dystrophy. This year his University of Leeds team has discovered two previously unknown recessive eye diseases originally thought to be variants of retinitis pigmentosa and that in cases of microcornea and cone-rod dystrophy the pattern of symptoms which present in patients are linked directly to mutations in their genes over time.

Our long-term aim remains to fund and equip an Eye Research centre in Yorkshire. There is both a wealth of research talent and diversity of papers originating in Yorkshire, but a dedicated centre is required if they are to be exploited to the full.

FORTHCOMING EVENTS

GARDEN PARTY 2011

Sunday 19 June 2011
3:00 to 6:00 pm

at Bourne House, Burrington,
south of Bristol – BS40 7AF

by kind permission of
Mr & Mrs Rodney Grey

Bourne House is a late Georgian country house with extensive gardens featuring well stocked flower borders, large lawns and spring fed stream at the foot of the Mendip Hills, there is a short woodland walk.



Bourne House

There will be a variety of interesting stalls and the Terry Hill Big Band will play and tea will be served.

LEGACIES AND IN MEMORIAM GIFTS

The charity's voluntary income is boosted by all those who make a gift in their **Will** through a **legacy**; this can reduce an Estate's liability to Inheritance Tax. We urge all our supporters to make a **Will** and are very grateful for all those who help eye research this way.

We thank all those who promote an "**In Memoriam**" collection in memory of a loved one;
a much longer lasting memory than a floral tribute.

Remember if you are a tax payer please ensure we have a "**Gift Aid Declaration**" so that we can claim back tax and boost the value of your gift. Higher rate tax payers can obtain additional tax relief.



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