

NATIONAL
EYE
RESEARCH
CENTRE
YOUR SIGHT
OUR VISION

NEWSLETTER

Spring • 2010

BRISTOL EYE HOSPITAL 200TH ANNIVERSARY

The **National Eye Research Centre**, based in the Bristol Eye Hospital, congratulates the hospital on being one of the leading eye hospitals in the United Kingdom in its 200th Anniversary Year. Much of the research supported by the Centre is done in the Bristol Eye Hospital



Bristol Eye Hospital

RESEARCH IN BRISTOL STRENGTHENED BY RETURN OF FORMER RESEARCH FELLOWS AS LECTURERS

The Division of Ophthalmology of the University of Bristol has had its research staff greatly strengthened by the return of Dr Richard Lee and Dr Denize Atan who were originally funded as Research Fellows by the **National Eye Research Centre** and have now been appointed Lecturers and able to devote more than half of their time to eye research. Articles follow covering their careers and research interests.

DEVELOPMENT OF RESEARCH IN BRISTOL

THE DIRECTOR OF RESEARCH, PROFESSOR ANDREW DICK WRITES:

I have previously focused in past newsletters on the support NERC gives to fundamental basic science research which is the foundation for progress to better care for our patients. This newsletter highlights the promise of translating such findings into clinical practice by showcasing individuals who have developed with NERC support, and are rapidly rising to be clinical academic leaders of the future and

maintain the momentum for advancement.

Although the road of development of new therapies or approaches to better care is often frustratingly long, it does happen and the national landscape is changing to facilitate more rapid progress within the NHS. Ophthalmology nationwide is a beacon of success with leading examples of new therapies for better care...

...including gene therapy, stem cells and new biologic drugs. NERC has helped support some of these aspects nationwide. In Bristol we are celebrating the 200th year of the Bristol Eye Hospital (BEH) and during the year we will be highlighting the care that has been provided regionally as well as where we are now, and where we will be going; all as a result of research and development in which NERC has and continues to be pivotal.

Moving toward better care requires a seamless platform and ability to conduct clinical research alongside NHS services. In BEH 200th year we will see refurbishment of clinical areas and a state of the art Clinical Research Facility to conduct clinical research trials alongside NHS services. This is thanks to the strong alliance and collaboration between the Universities Bristol Hospital NHS foundation Trust and University of Bristol.

DR DENIZE ATAN

CLINICAL LECTURER, DEPARTMENT OF OPHTHALMOLOGY, UNIVERSITY OF BRISTOL



Dr Denize Atan

Denize Atan is an academic ophthalmologist with a special interest in genetics. She currently works as clinical lecturer in ophthalmology at the Bristol Eye Hospital and bases her research in the Department of Cellular and Molecular Medicine at the University of Bristol.

Denize conducted her undergraduate medical training in Oxford and Cambridge, followed by postgraduate specialist training in Medicine and Ophthalmology in Oxford and the South West of England. However, her interest in genetics was ignited in Bristol, when she joined the Molecular Ophthalmology Group, headed by Dr Amanda Churchill. Here, she embarked on a project investigating the influence of genetic variants on our susceptibility to inflammatory eye disease, namely uveitis, in

In the clinical research unit we conduct studies that investigators design to promote better understanding of impact of eye disease, interrogate mechanisms and biological pathways that lead to disease and drug trials. This is possible because of the academic strength within BEH staff and academic leadership within the University of Bristol. Our drug trials look at possible better therapies for age related macular degeneration, diabetes and inflammatory disease (uveitis and thyroid eye disease). These are led by either investigators in Bristol or we form part of a multi-centred trial led by other institutions and Universities. Such networks and collaboration are pivotal to success of trials and translation of new therapies. All ventures to various extents require collaborative support between charity, industry and the NHS. NERC plays an essential role nationwide to make this happen.

collaboration with Professor Andrew Dick, which led to the discovery that specific variants of the Interleukin 10 (IL10) gene are associated with our susceptibility to uveitis. Since experimental models of uveitis have shown that IL10 has anti-inflammatory properties, promoting tolerance and dampening down the inflammation in uveitis, genetic variants which might influence the timing and amount of IL10 produced during the induction of disease, could explain why some people are more vulnerable to developing inflammatory disease than others, and provide a link between models in the lab and patients in the clinic. This research was funded by NERC, together with The Wellcome Trust and Medical Research Committee of the United Bristol Hospitals Trust, who helped Denize bring her results to publication and complete her PhD thesis in 2008.

Following her initial successes, Denize then endeavoured to develop her conceptual and technical expertise in genetics further with a post-doctoral research fellowship at the Hospital for Sick Children in Toronto, an internationally renowned centre of excellence in clinical and basic science research, and under the supervision of Rod McInnes, Professor of Molecular Genetics and Paediatrics at the University of Toronto, Alva Chair in Human Genetics at McGill University, and President-Elect of the American Society of Human Genetics. Funded by The Wellcome Trust, her research delved into the genetic network responsible for neuronal development in the eye and the role of transcription factors, proteins that regulate gene expression. One such transcription factor, Prdm8, is required for the maintenance of a major class of retinal interneuron: the rod bipolar cell which relays visual signals from rod photoreceptors

to the optic nerve. The absence of Prdm8 and rod bipolar cells in experimental models, mimics a type of blindness that is first diagnosed in children - congenital stationary night blindness. The aim of ongoing research is to place Prdm8 within the network of genes that control interneuron development and to discover how this might relate to inherited causes of blindness in children.

With the help of funding from NERC, Denize will be continuing this research in Bristol where she will benefit from the support and resources available through Bristol Neuroscience (MRC

centre for synaptic plasticity, Laboratories for Integrative Neuroscience & Endocrinology, Institute of Clinical Neurosciences), the Wolfson Bioimaging facility, Bristol Vision Institute, the Bristol-Cardiff Neuroscience Collaboration and the Bristol-Bath Developmental Biology Club. Furthermore, in collaboration with the Bristol Retinal Neural Progenitor Cell Group (Dr Maeve Caldwell and Dr Tina Qui), she will be able to ask whether neural progenitors may be manipulated to repopulate lost bipolar cell populations and to determine whether this might be a therapeutic option in the future.

DR RICHARD LEE

CLINICAL LECTURER, DEPARTMENT OF OPHTHALMOLOGY, UNIVERSITY OF BRISTOL

Mr Richard Lee was appointed as a NERC Clinical Research Fellow in 2004. Prior to this he had undertaken 3 years Basic Surgical Training at the Yorkshire School of Surgery and 4 years Ophthalmic Specialist Training in Yorkshire and Bristol. On completion of his fellowship in 2008 he was awarded a Clinical Lectureship funded by the National Institute for Health Research (NIHR), enabling him to embark on a career in academic ophthalmology where he promises to make a significant national and international contribution to vision research.

As part of his Clinical Research Fellowship he wrote a PhD thesis which was nominated for an award by the University of Bristol's Faculty of Medicine and Dentistry under the supervision of Professor Andrew Dick. This examined ways of minimising the use of steroids in patients who risk losing their vision to uveitis – an inflammatory condition of eye, and a common cause of blindness in the working age-group. Steroids have many unwanted side-effects, and his work has demonstrated that 60% of patients can be spared long-term reliance on steroids if they are taking another medication called Tacrolimus. He also demonstrated that patients who do not respond well to steroids, and consequently suffer prolonged high-dose treatment, have a particular type of steroid resistant white blood cell. He went on to characterize these cells and this knowledge is being used to develop diagnostic tests and personalised treatments for steroid resistant patients.

During the course of his NERC Clinical Research Fellowship Richard published 11 peer-reviewed papers in scientific journals and this has attracted interest from both academia and industry. Reflecting this, he was invited in 2009 on a visiting fellowship to the National Institutes of Health (NIH) in the United States where he worked with an internationally renowned team of clinicians and scientists, led by Dr Bob Nussenblatt, to further his studies of ocular inflammatory

diseases. This involved the application of cutting edge technologies to investigate variations in the expression and control of genes in the white blood cells of patients with uveitis. As a result, an ongoing collaboration with the NIH has been established and joint studies benefiting from the combined research expertise and clinical services in Bristol and Washington DC are now underway.

With NERC's support Richard is developing into a clinical academic leader of the future, and this has been recognised by his appointment to a NIHR Clinical Lectureship. He is now establishing an independent programme of research with his own research team through which he is continuing to advance knowledge in the study of inflammatory eye conditions for the long-term benefit of patients who suffer from these blinding diseases. Hence, by supporting outstanding individuals such as Richard, NERC is securing a future for vision research in the UK.



Dr Richard Lee

EYE BANKING, CORNEAL TRANSPLANTATION AND CORNEAL GRAFT REJECTION

BY PROFESSOR JOHN ARMITAGE

A clear cornea is essential for normal vision. Loss of corneal transparency through disease or damage causes severe visual impairment but this can be treated successfully by a corneal transplant. In the 1980's the University of Bristol set up the first Corneal Transplant Service Eye Bank with the help of the **National Eye Research Centre**. With its sister bank in Manchester, this NHS-funded service supplies approximately 3,000 corneas a year for sight saving operations in hospitals throughout the UK.

Although most corneal transplant operations initially restore sight, more than 40% of them fail in the long term (10 years or more). Graft rejection, where the body identifies the graft as 'foreign', is a major cause of failure. The Centre is supporting a long term study in patients to evaluate the advantages of tissue matching between donors and recipients as a means of avoiding rejection. The Centre is also supporting laboratory research to further our understanding of the mechanisms of corneal transplant rejection. This research will lead to better

prediction of the risk of rejection and better treatments to combat its effects should it occur.



Corneas being evaluated in the Eye Bank

TEARS PROTECT US FROM BUGS

BY DR MONICA BERRY

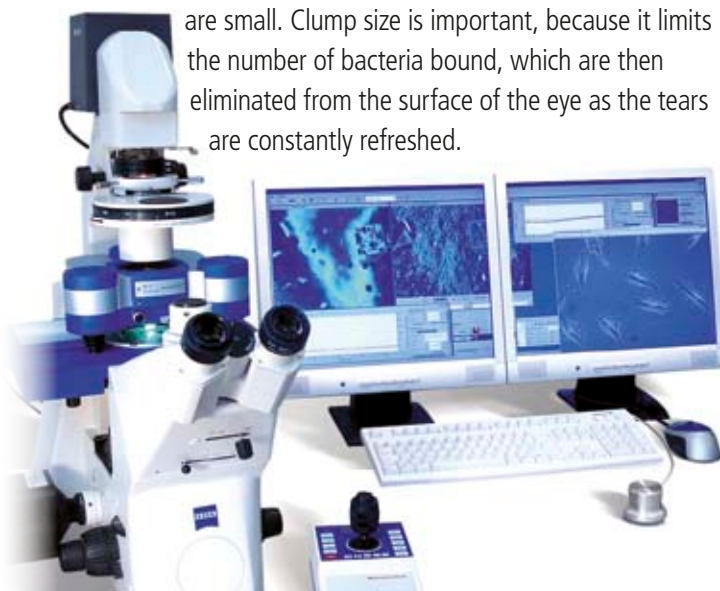
We are happy hosts to lots of bacteria, which take part in the normal functioning of our bodies. How these organisms are selected and kept at bay is an evolutionary tale worth unravelling.

The molecules which bugs recognise are often sugars, at the end of sugar chains. At the surface of the eye most of these sugars are sialic acids. We have shown that purified mucins are

especially rich in a particular sialic acid, while our colleagues in Boston found that a different sialic acid dominates in the tears as a whole. To solve the conundrum, Sarah Baos, a graduate student shared by Physics and the Academic Unit of Ophthalmology, used an Atomic Force Microscope to map the distribution of the two sialic acids. We confirmed the previous results: the two types of sialic acids are not distributed evenly on mucins and other sugary molecules. More, and more interestingly, we also found that the clumps of sialic acids that bind potentially damaging bacteria are small. Clump size is important, because it limits the number of bacteria bound, which are then eliminated from the surface of the eye as the tears are constantly refreshed.



Sarah Baos



YORKSHIRE EYE RESEARCH - Tel: 0113 292 2837

Eye Department, Clarendon Wing, Leeds General Infirmary, Leeds LS2 9NS

Appeal Administrator: Ms Susannah Voke

After a difficult first half of the year for fundraising, there has been a notable increase in voluntary income and some welcome grants received.

During 2009 we have funded research into the causes, prevention, detection and treatment of Age-related Macular Degeneration (ArMD), Glaucoma and Diabetic Retinopathy which affect so many of our elderly and funded the first phase of a three year study into inherited Retinitis Pigmentosa, Microcornea and Cone Rod Dystrophy; all major causes of blindness endured by young children.

The next year will see us support research to improve the treatments available to children with Retinoblastoma, a particularly nasty form of eye tumour and research to determine why premature babies are at risk of going blind. This will result in better diagnostic techniques.



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

FORTHCOMING EVENTS

GARDEN PARTY 2010

Sunday 27 June 2010
3:00 to 6:00 pm

at Cotswold Farm,
Duntisbourn Abbots, near
Cirencester, Gloucestershire,
GL7 7JS

by kind permission of
Mrs Mark Birchall

Cotswold Farm, dating back to the 17th Century, has extensive gardens overlooking a beautiful valley. There will be a variety of interesting stalls, the opportunity for our supporters to have items of interest valued by Moore, Allen & Innocent, a Silver Band will play and tea will be served.



Cotswold Farm, Duntisbourn Abbots

LEGACIES AND IN MEMORIAM GIFTS

The charity benefits greatly from those who leave a gift in their Will. These gifts have funded much needed research equipment and the salaries of research workers. Remember, a legacy can reduce an estates liability to Inheritance Tax.

In Memoriam gifts in aid of a loved one have much longer lasting benefits than floral tributes.

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 by 28p in the £1. Higher rate tax-payers can obtain further relief.



Bristol Eye Hospital,
Lower Maudlin Street,
Bristol BS1 2LX
Telephone: **0117 929 0024**

Member of the Association of Medical Charities

You can also reach NERC by...
Fax: **0117 925 1421**
Email: nerc-charity@bristol.ac.uk
Website: <http://www.nerc.co.uk>

