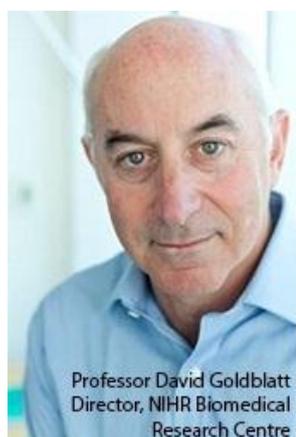


**News from the National Institute for Health Research  
Biomedical Research Centre at  
Great Ormond Street Hospital for Children NHS Foundation Trust  
and University College London**

**November 2014**



Welcome to the November edition of our National Institute for Health Research ([NIHR](#)) Great Ormond Street Hospital (GOSH) Biomedical Research Centre (BRC) newsletter, which is designed to highlight our notable activity.

It is a great pleasure to welcome our new BRC manager, Dr Katie Payne who joins us on 1 December. Katie has been at Imperial College London where she managed two British Heart Foundation funded research centres in cardiovascular science.

Congratulations to Professor Adrian Thrasher on being awarded a Wellcome Trust Principal Fellowship; this is the Wellcome Trust's most prestigious personal award and provides long-term support for researchers of international standing. Adrian heads the BRC's Gene, Stem and Cellular Therapies theme.

In this newsletter, you will find a new section focusing on training, one of the core functions of a BRC. We deliver training at a national level and to multiple disciplines. As an example of how we fulfil our national training remit, please read the article on a training weekend for paediatric doctors that we funded and organised in September. An update on our training strategy for nurses and Allied Health Professionals can also be found in this section.

The inaugural BRC Open Day for the general public took place on a Saturday in November and saw close to 200 members of the public sign-up to learn about our BRC activity. The day was a huge success, please read more about it in our patient and public section.

Professor Dame Sally Davies, the Chief Medical Officer and Chief Scientific Advisor, visited GOSH/Institute of Child Health (ICH) to deliver a Otto Wolff lecture, please read about her talk on biomedical research in the special feature section.

I hope you enjoy reading this newsletter and as always welcome any thoughts and contributions you would like to make.



David Goldblatt  
Director, NIHR GOSH BRC  
Director, Clinical Research and Development  
Professor of Vaccinology and Immunology  
Visit our [website](#)

## General news

### **BRC researchers win UCL's Therapeutic Innovation Fund awards**



We are pleased to announce that that BRC researchers at ICH have been awarded three out of five of UCL's Therapeutic Innovation Fund (TIF) awards and one out of seven MRC Confidence in Concept (CiC) fund awards. We congratulate the three TIF award recipients: Dr Kenth Gustafsson, Professor Jennifer Morgan and Dr Chris O'Callaghan; and the CiC award recipient: Professor Bobby Gaspar.

There was tough competition with over 30 applications submitted for each scheme. TIF awards are supported by funds from all three NIHR BRCs at UCL. The award provides seed funding to support biomedical innovations at their earliest stage of discovery research. Both schemes are co-ordinated by the [Translational Research Office](#).

The CiC awards are funded by the Medical Research Council (MRC) to support the UCL's translational research projects. The aim of the fund is to support preliminary work or feasibility studies to establish the viability of a novel approach. This should accelerate the transition from discovery research to translational development projects which will be suitable to apply for main stream translational funding such as the MRC Developmental Pathway Funding Scheme.

### **GOSH BRC seminar on 2 October 2014**



The October seminar, chaired by Professor Phil Beales BRC theme lead for Molecular basis of childhood disease, showcased the multi-disciplinary nature of research taking place at the BRC and in the wider organisations of GOSH and ICH.

The first speaker was Dr Kate Oulton, BRC Clinical Academic Programme Lead: Nursing and Allied Health Research. Her talk gave an insight to NIHR's support for nurses and AHPs as researchers. Talks followed by Dr Kate Khair, a Nurse Consultant at GOSH, on 'Living with haemophilia – what children tell us', Ms Victoria Selby, a physiotherapist and PhD student, and Danielle Ramsey, a research physiotherapist, on 'Recent

Developments in Outcome Measures for Children with Neuromuscular Disorders', Ms Sonja Soskic, a BRC funded PhD student, on 'Advanced imaging in cerebral palsy' and Dr Claire Booth, an academic clinical lecturer, on 'Gene therapies for rare diseases: translation to clinical benefit'.

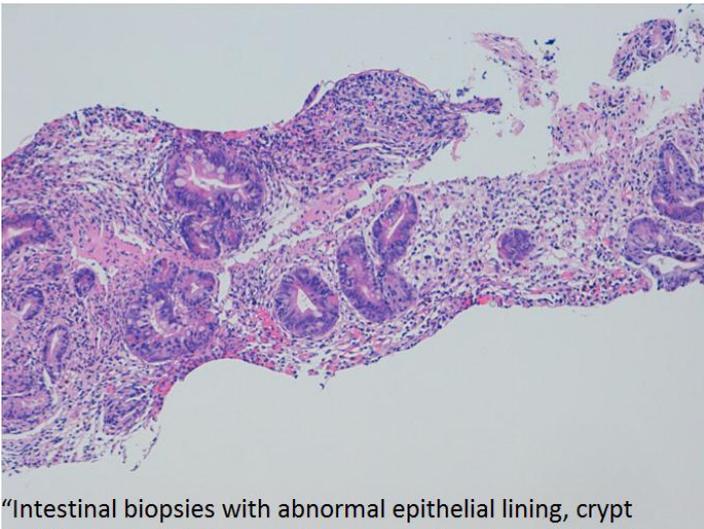
The next BRC seminar will take place on Wednesday, 21 January 2015, please find further details in the [events section](#).

## **Molecular basis of childhood disease theme news**

### **BRC and Harvard collaboration provides new insights into mechanisms behind renal cysts**

In collaboration with Harvard Medical School, a research group led by Professor Phil Beales, a GOSH BRC theme lead has discovered the molecular basis of a common phenotype - renal cysts, of two different conditions grouped under the genetic disorder of [ciliopathies](#). Renal cysts are both displayed in Bardot–Biedl syndrome (BBS) and autosomal dominant polycystic kidney disease. The findings reveal novel insights in the signalling pathway that is controlled by a complex called the BBSome. The study published in the journal [Human Molecular Genetics](#) suggests that a mistargeted PC1 protein is at the origin of renal cysts.

### **Successful collaboration continues for the BRC funded GOSgene facility and the North East Thames Regional Genetics Service**



“Intestinal biopsies with abnormal epithelial lining, crypt architectural distortion and presence of acute and chronic inflammatory cells in a patient with VEOIBD”

The development of molecular diagnoses is of prime importance in a time with constantly emerging novel genotype-specific therapies. The GOSH BRC funded gene discovery facility, [GOSgene](#) and its collaborator, the North East Thames Regional Genetics Service, are continuing to successfully develop screening tools for genetic diseases.

In a recent publication in the [Journal of Medical Genetics](#), the collaborative partners report results on their development of a gene panel to screen patients affected by very early on-set inflammatory bowel disease (VEOIBD). The development of this panel is significant, because of its impact on patient management. It can identify in a short period of time which patients have certain VEOIBD genotypes and advise on the correct treatment pathway, e.g. haematopoietic stem cell transplantation. At

the same time, whole exome sequencing was performed by GOSgene in the same VEOIBD patients and the results compared with the gene panel.

### **Discovery of the molecular basis of a new intellectual disability syndrome**



Professor Phil Stanier

A collaboration led by Professor Phil Stanier and involving several other co-workers at the GOSH BRC as well as three European universities has led to the discovery of the molecular basis of a new intellectual disability/cerebellar ataxia syndrome.

These phenotypes occur together in a large number of genetic conditions, sometimes including epilepsy, and are consistent with a small cerebellum. This research has shown that mutations in a gene called SNX14 leads to a distinct and recognisable syndrome. This is characterised by poor development and maturation of the cerebellum, associated with ataxia, absent speech and hearing loss. The findings from the research study leading to this discovery were published in [The American Journal of Human Genetics](#).

## Gene, stem and cellular therapies theme news

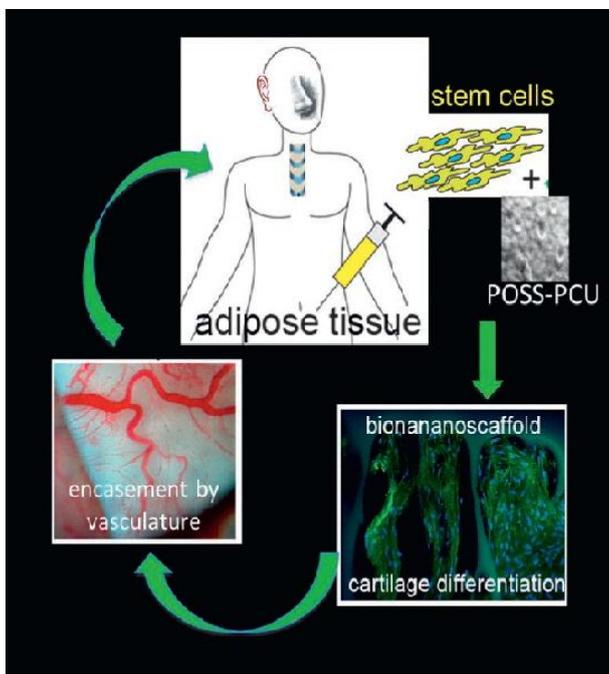
### **BRC achieves safer gene therapy for x-linked severe combined immunodeficiency**

GOSH BRC theme lead Professor Adrian Thrasher and a team of local and international collaborators have developed improved gene therapy technology for treatment of children with X-linked severe combined immunodeficiency (X-SCID) who do not have matched bone marrow donors.

X-SCID is an inherited disorder of the immune system that affects predominantly boys. Most children die before they are one year old from infections that their immune system is unable to fight.

A clinical trial published in the journal [New England Journal of Medicine](#) used a modified Gamma Retrovirus Vector to treat the condition and restored immunity in most patients. The treatment showed high efficacy and better outcomes for most patients with fewer adverse effects. The new therapy was covered by the [BBC news](#).

### **Research underway to use stem cells in ear reconstruction**



Paediatric adipose tissue-derived stem cells (ADSCs) home inside nanocaged POSS-PCU and undergo chondrogenic differentiation, as indicated by collagen II expression (green). The resulting ADSC-POSS-PCU bionanoscaffold is efficiently encased within a vascular network. This new bionanoscaffold represents a promising tool for autologous cell-based tissue engineering aimed at repairing cartilages, such as ear, nose and tracheal cartilage.

Dr Patrizia Ferretti, an ICH researcher with links to the BRC, has been working on a study funded by the [Newlife Foundation for Disabled Children](#) that in the near future aims to enable the use of stem cells derived from a patient's own fat to create a new ear. This would be far less invasive than the current procedure which involves using part of the patient's rib cartilage to reconstruct the ear and where the new skeletal structure can still suffer occasional rejection by the patient's immune system.

GOSH carries out more ear constructions than any other UK hospital. Ear reconstructions bring about big improvements to the quality of life of children with abnormally small ears. Read the full article in the [GOSH press release](#). The [BBC news](#) also covered the story earlier in the year.

Footnote to image on the left: This image was published in *Nanomedicine: Nanotechnology, Biology, and Medicine*, Volume 10, Number 2, L. Guasti, B. Vagaska, N. W. Bulstrode, A. M. Seifalian, P. Ferretti, Chondrogenic differentiation of adipose tissue-derived stem cells within nanocaged POSS-PCU scaffolds: A new tool for nanomedicine, Pages 279-289, Copyright Elsevier (2014).

## Novel therapies for childhood disease theme news

### **BRC supported research demonstrates effectiveness of the new 13-valent pneumococcal vaccine and defines new correlates of protection**

A study led by NIHR GOSH BRC Director, Professor David Goldblatt, in collaboration with Public Health England and published in the journal [The Lancet Infectious Diseases](#), has shown that a new 13-valent pneumococcal conjugate vaccine, introduced into the infant immunisation programme on 2010, provides significant protection for most vaccine serotypes. This is the first report of this new vaccine's effectiveness and incorporated an indirect cohort method to assess vaccine effectiveness in the 3.5 years following introduction. The paper also defined, for the first time, new correlates of protection for extended pneumococcal conjugate vaccines that will inform future vaccine licensing strategies and implementation of PCVs around the world.

This report is independent research commissioned and funded by the Department of Health Policy Research Programme (National Vaccine Evaluation Consortium, 039/0031). The views expressed in this publication are those of the author(s) and not necessarily those of the Department of Health.

*Streptococcus pneumoniae* (pneumococcus) is a leading cause of serious illness, including meningitis and pneumonia among children and adults worldwide. Following changes in pneumococcal disease causing serotypes, a new 13-valant pneumococcal vaccine has been used to combat the disease.

## First UK application of a novel kidney transplantation method at GOSH

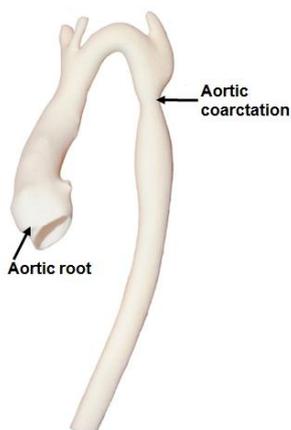


For the first time in the UK, a novel kidney transplantation method has been performed at GOSH. This method is used for patients having previously had transplants. The result of having had a transplant before is that the body will have produced antibodies that can jeopardise future transplanting success by fighting any introduced foreign objects. The new method removes a large proportion of the antibodies using a blood filtering process called plasmapheresis. Subsequently, the blood is re-introduced into the patient; however due to the fact that not all antibodies can be removed, the patients still need to take strong drugs to prevent their immune system from rejecting the kidney.

BRC supported Consultant, Dr Stephen Marks said that "kidney transplantation offers the best quality and quantity of life for children with severe irreversible kidney failure and the new technique could make transplants possible in these children where they weren't before, avoiding their reliance on dialysis." The full story can be read in the [GOSH press release](#).

## Diagnostics and imaging in childhood disease theme news

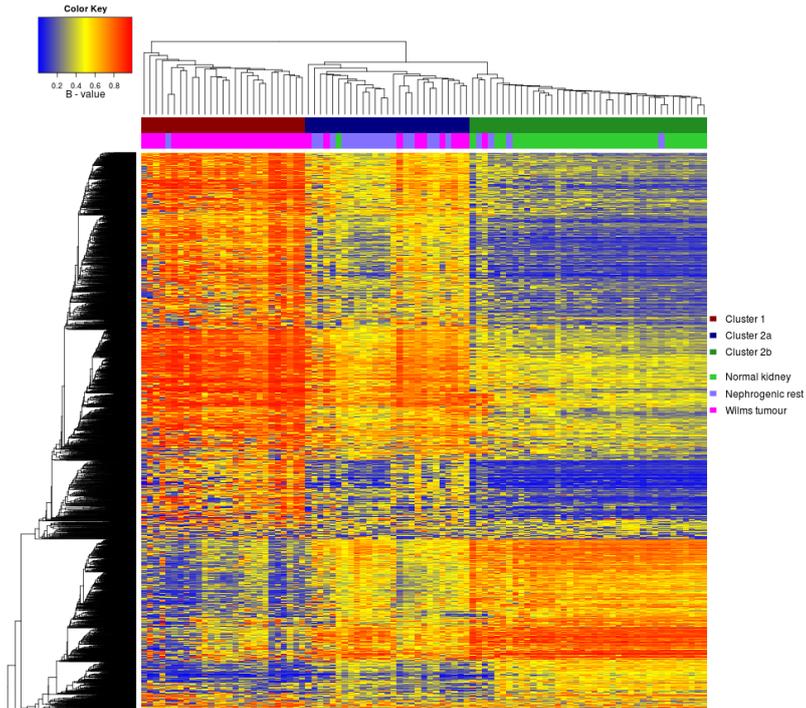
### Public engagement award to BRC supported research centre at GOSH



The Centre for Cardiovascular Imaging based at GOSH has been awarded a UCL Beacon Bursary for public engagement. The funding will allow the team to undertake a range of projects engaging a small group of teenagers and their parents to improve communication between clinicians and patients about congenital heart defects. The first project will assess whether 3D models of congenital heart defects can help the patients better understand their condition and what it entails. Read more about the use of the funding in the [UCL news](#).

The Beacons for Public Engagement is a UK initiative to promote excellence in public engagement amongst higher education institutions and encourage a culture change to recognise, reward and support public engagement. Funding is provided by the Higher Education Funding Council for England, Research Councils UK and the Wellcome Trust.

## Encouraging research into liquid biopsy use for Wilms tumour diagnosis and treatment



**Heatmap of clustered methylation levels in normal kidney, nephrogenic rest and Wilms tumour tissues**

planning. A Q&A in [Biome, BioMed Central's online magazine](#) answers further specific questions on the implication of this research for patients with Wilms tumour.

Jocelyn Charlton, a PhD student supervised by GOSH BRC supported Professor Kathy Pritchard-Jones, together with colleagues, has published research findings in [Genome Biology](#) describing an epigenetic biomarker in Wilms tumour tissue that could be detected in the circulation of patients with Wilms tumour.

Wilms tumour is the most common paediatric kidney cancer and there is a clinical need for a molecular biomarker to assess treatment response and predict relapse. A molecular biomarker detectable through liquid biopsy would also represent a much less invasive way to diagnose the subtype of renal tumour and predict its response to chemotherapy prior to surgery to obtain histology. This has the potential to improve treatment

### SPECIAL FEATURE

#### Chief Medical Officer and Chief Scientific Adviser lecture on “*Biomedical research now*”



**Professor Dame Sally Davies**

Professor Dame Sally C. Davies FRS FMedSci, Chief Medical Officer and Chief Scientific Adviser at the Department of Health, on 8 September 2014 delivered a compelling lecture on “Biomedical research now” as part of the Otto Wolff lecture series at UCL Institute of Child Health. The lecture provided insights into the UK government’s position on the biomedical research funding. Dame Sally explained how funders fit together and the NIHR’s role, the importance of translational research for achieving direct patient benefit, and about Genomics England and the challenges for the 100,000 whole genomes project. A key message was about how NIHR infrastructure, such as the NIHR GOSH Biomedical Research Centre, is supporting research by other funders, and helping to attract investment in the UK Life Sciences Industry.

## PATIENTS AND THE PUBLIC

### BRC Open Day in conjunction with the London Science Festival: 15 November 2014



For the first time ever, on Saturday 15 November, a BRC Open Day was held in conjunction with the London Science Festival. The event took place in Institute of Child Health, in two sessions, from 10:00-12:00, and 14:00-16:00. Several activities and seminars took place, with the aim of demystifying clinical trials and paediatric experimental medicine. Activities included such things as laboratory tours, looking at different types of cells under a microscope, making 'DNA' bracelets, a strong-man competition, dressing up to 'perform' gene and cell

therapy, and many others. Two hundred people attended the day, and commented that it was, 'Way better than football!', and 'Brilliant. Very interactive for the kids', and 'Excellent organisation and all staff were fantastic with attitude and effort.' Based on the success of the day, it is anticipated that the event will be run again next year.

### Life skills award: our Young Persons Advisory Group is working with the National Children's Bureau

Our Young Persons Advisory Group (YPAG) is working with the National Children's Bureau on an accreditation, called a 'Life Skills Award'.

Our YPAG group is an invaluable resource for our BRC researchers.

If you have a research study that you would like to present to the YPAG for their input (for example how information leaflets are worded, or to comment on the design of a study, or your dissemination plan), please contact [Dr Erin Walker](#) (BRC lead for Patient and Public Involvement and Engagement in research).

## TRAINING

### Residential National Paediatric Academic Trainee Weekend September 2014

Residential National Paediatric Academic Trainee Weekend at Ashridge Business School



On 13-14 September the first Residential National Paediatric Academic Training weekend organised by the GOSH BRC was held at Ashridge Business School. 40 academic trainees at all levels attended the event from training centres all over the UK. The weekend provided a unique opportunity to develop research skills, from encouraging the involvement of young people in the design of your research to reviewing grant proposals, as well as networking with peers and senior academics.

There was a great atmosphere of interaction and delegate involvement during the whole weekend. The weekend was a huge success with delegates rating the quality of education as excellent and stating they would recommend future weekends to colleagues. Hadeel Hassan, a delegate from the weekend, writes about her five top tips from the weekend in her [blog](#). Read the full report by our trainee lead for the weekend, Dr Catherine Wedderburn, on [our website](#).

## **First outputs achieved by our training strategy for nurses and Allied Health Professional**

As part of the BRC's training agenda, the recent appointment of Dr Kate Oulton to Clinical Academic Programme Lead: Nursing and Allied Health Research, has already shown outputs. Kate's first initiative was a call for applications from nurses and Allied Health Professionals (AHPs) to undertake research internships (up to one day a week funding for 6 months) to support applications for NIHR Clinical Doctoral (PhD) Research Fellowships. Four awards have been made. A similar internship is planned for 2015 for nurses and AHPs wanting to apply for the NIHR Doctoral (non-clinical) Fellowship.

## **EUREKA Event in Translational Medicine on 4 September 2014**

The [EUREKA Institute](#) is an institute concerned with exploring best avenues to deliver training to new professional in translational medicine. A half-day event was hosted by GOSH BRC supported and EUREKA alumni Professor Lucy Wedderburn at University College London (UCL) Institute of Child Health (ICH). The event aimed to 1) inform UCL staff of resources available at UCL to support UCL researchers in the development of translational medicine pathway and 2) introduce a new network called EUREKA that involves UCL as a building partner.

The event featured talks on translational medicine by Professor Phil Hawkins and Dr Chiara Bacchelli and an overview of services provided by UCL support departments of [UCL Business](#), [Research and Innovation](#) and [Translational Research Office](#).

Over 40 attendees attended the event and the feedback was excellent. In late 2014, there will be a further two training days for EUREKA alumni and the planning of a larger EUREKA-Lite event in 2015, which will be open to all to apply for.

## **Summer students at the BRC**

At the BRC we take our research capacity building function very seriously and [target a number of groups](#). One of our schemes is aimed at aspiring scientists who are keen to gain experience in a research laboratory over the summer. We assist them with their skills development and offer insight to a real-time professional scientific environment in a world-leading research Institute. Over the summer we opened our doors and welcomed students from other academic institutions nationwide, in the hope of inspiring them to pursue scientific careers.

We have been able to accommodate a number of summer students this year, both funded through our BRC and self-funded. A report from one of the students can be found on [our website](#).

## **EVENTS**

**8 December 2014, 13.00– 14.00, Kennedy Lecture theatre, UCL Institute of Child Health**

**Otto Wolff lecture: Involving children and young people to improve our research**

Speakers: Dr Jennifer Newman and Dr William van 't Hoff, Medicines for Children Research Network

**Workshop series supporting nurses and Allied Health Professionals in their application to the NIHR Masters in Clinical Research (MRes)**

For dates and workshop topics, please visit our [website](#)

Contact: [Dr Kate Oulton](#) for more information and to book for free space (available only for GOSH nurses and [NIHR eligible Professions](#) at GOSH).

**21 January 2015, 12:00–13.30, Kennedy Lecture theatre, UCL Institute of Child Health**

**GOSH BRC Seminar**

Chair: Professor Adrian Thrasher.

Speakers include Professors Kathy Pritchard-Jones and Steve Hart.

Followed by lunch in Winter Garden after 13:30

**6 May 2015, 14:00–18.30, Kennedy Lecture Theatre, UCL Institute of Child Health**

**GOSH BRC symposium**

The 2015 BRC symposium will have two foci, one on local clinicians and scientists and one on our patients and their carers, members of the general public and organisations supporting our research. The programme will include lectures for our research community between 2 and 4.40pm and then short talks for the wider community, including school children, between 5 and 6.30pm. A programme will be available in early 2015.

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