National Institute for Health Research

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

National Institute for Health Research (NIHR) Great Ormond Street Hospital Biomedical Research Centre (BRC) newsletter April 2014


Professor David Goldblatt
Director

Welcome to the latest edition of our newsletter which will bring you the latest news from the NIHR Great Ormond Street Hospital BRC.

I would like to congratulate Professors Lyn Chitty, Neil Sebire and Phil Beales on having received NIHR Senior Investigator awards. NIHR Senior Investigators represent the country's most outstanding leaders of clinical and applied health and social care research. They join me as well as Professors Adrian Thrasher, Rosalind Smyth, Catherine Law as Great Ormond Street Hospital (GOSH) / University College London (UCL) Institute of Child Health (ICH) based NIHR Senior Investigators.

Professor Dame Sally Davies (Chief Medical Officer) has recognised the hard work of our researchers and clinical staff by providing a quote to accompany our story on first global patient recruitment to four clinical trials at GOSH. Please view the full story below.

This edition includes examples of our new high impact programmes, treatments, research, study awards, and clinical trial impacts. Particular highlights include the discovery of a new treatment that improves lives for patients with hyperinsulinemic hypoglycaemia and new funding for a study aiming to beat childhood brain tumours. Findings have been made on factors influencing babies' birth weights, which in turn can be used to inform the monitoring of high risk pregnancies. Recently, GOSH has received thanks from BioMarin for contributing to the regulatory approval of a new treatment for Morquio A syndrome, a rare lysosomal storage disease.

In addition to the stories that appear in our newsletter, you can also see more information about our BRC on our redesigned website.

We would like to ask you to help us evaluate our BRC newsletter and get your views on our new website. Please follow this link to SurveyMonkey and complete our short questionnaire. Please e-mail BRC.newsletter@gosh.nhs.uk with any future contributions to the newsletter you would like to make.

David Goldblatt
Director, NIHR Biomedical Research Centre
Director, Clinical Research and Development
Professor of Vaccinology and Immunology
Visit our new website

General news

GOSH BRC agrees funding for a high impact collaborative project with Miltenyi Biotech
GOSH BRC is co-funding a £1.4m collaborative project with Miltenyi Biotec that will aim to improve the efficiency and effectiveness of T cell modification and to develop automation of the T-cell transduction process. This will allow for large scale manufacture of gene and cell therapy products. The project will support GOSH/UCL's position as a major European hub of gene and cell therapy technology. Dr Waseem Qasim, who is leading the project for the BRC said: 'We are very excited about working with Miltenyi to adapt a closed system robotic device that can collect immune cells from a blood donation and grow them in a specialised culture chamber before automated enrichment using microscopic magnetic beads. The introduction of steps that allow cells to be genetically engineered using the device should help widen the application of gene therapy technology beyond the handful of centres that currently have the necessary clean room facilities.'

NIHR congratulates GOSH on first global recruits
We were extremely pleased to hear that research teams at GOSH recruited the first global patients to four multi-centre studies, including the first two patients to a Summit PLC sponsored phase Ib study. The treatment under investigation in this phase Ib study is a compound capable of up-regulating the production of utrophin, a protein that can compensate for the lack of dystrophin, which cannot be produced in boys with Duchenne Muscular Dystrophy (DMD). This treatment could slow or even stop the progression of this devastating condition. Read the full press release by Summit PLC for more information. This is a significant achievement and shows the dedication of the research and research support teams in the Trust. Professor Dame Sally C. Davies, Chief Medical Officer and Chief Scientific Adviser at the Department of Health said: 'I am really pleased to hear that research teams supported by GOSH recruited the first global patients to four industry multi-centre contract research studies tackling a number of important diseases, including a study into a potential new treatment for boys with DMD. Research such as this has the potential to save lives. These global firsts are a significant achievement and shows the dedication of the research and research support teams at GOSH. This achievement also demonstrates the impact of the measures we are putting in place to ensure that the UK stays internationally competitive as a place to undertake high quality life sciences research.'

GOSH BRC seminar event on 25 February 2014


UCL Institute of Child Health winter garden

The second GOSH BRC seminar, chaired by Professor Neil Sebire, was held on 25 February in the Kennedy Lecture Theatre at ICH. One aim of the BRC seminars is to facilitate future collaborative work between groups across GOSH and UCL and for individuals to maximise the use of the research infrastructure supported by GOSH BRC. Speakers and attendees had the opportunity to talk to each other, over lunch, about potential future collaborations. The event attracted more than 100 people from GOSH and UCL and feedback was very positive.

The first speaker, Dr Kevin Mills, gave the audience an insight into the BRC-funded GOSomics facility that is driving forward proteomics, metabolomics and lipidomic analysis at UCL ICH. The second presentation was given by Professor Paul Gissen and Dr Manju Kurian, who described their translational research in neurometabolic syndromes in childhood and highlighted how their work will deliver future benefits to patients. Dr Miho Ishida talked about efforts to identify genetic and epigenetic factors that cause fetal growth abnormalities, such as Silver-Russell Syndrome in Professor Gudrun Moore's group. Dr Paolo De Coppi described his recent work on amniotic fluid stem cells and tissue regeneration. Dr Fiona Chan-Porter gave an introduction to the grants advice service available through the UCL Translational Research Office.

Take home messages from the NIHR event: Celebrating Clinical Research Nurses


Speaker: Dr Susan Hamer (NIHR Director of organisational and workforce

On 5 February, following on from the success of last year's NIHR-hosted clinical research nurse event, the NIHR held a series of regional events. These events were to 'celebrate the care nurses bring to the patient experience, the leadership they bring to the delivery of research and the innovation nurses bring to the clinical research field'. Four delegates from GOSH were able to attend this event, which they found most inspiring. Loraine Hodsdon, our Head of Nursing Clinical Research, gave a presentation about the 'paediatric perspective-development of a paediatric research team'. Events like these acknowledge on a national level the importance of nurses in the delivery of research studies and allow nurses to share experiences and meet other inspirational co-professionals. The event also covered the 6Cs Nursing strategy launched by the Chief Nurse for England in December 2012. This strategy asks all NHS staff to embrace values of care, compassion, competence, communication, courage and commitment in their work.

Prestigious fellowship in translational medicine awarded to BRC Research Associate


Dr Wendy Heywood

We are pleased to announce that BRC Research Associate, Dr Wendy Heywood, has received a fellowship from UCL to attend the Eureka Institute for Translational Medicine and undertake their 6th annual international certificate program. The Eureka Institute's mission is to educate new professionals in translational medicine. Through the fellowship programme, Dr Heywood will be supported by international leaders in her work to address challenges posed in the field of translational medicine. Translational medicine seeks to bridge the gap between the discovery of new diagnoses and treatments and their development into novel therapies for human diseases leading to patient benefit.

Molecular basis of childhood disease theme news

Newly discovered treatment improves lives for patients with hyperinsulinemic hypoglycaemia

Hyperinsulinemic hypoglycaemia (HH) is a condition causing low blood glucose levels through the excessive production of insulin. It is the most common cause of severe, persistent neonatal hypoglycaemia and in its most severe form the condition can be life-threatening. If severely affected patients do not respond to the standard medication (diazoxide), removal of the pancreas is the only treatment, resulting in the lifelong need for insulin injections and pancreatic enzyme replacement therapy, which is necessary to enable the supply of enzymes responsible for digestion. BRC-supported clinician Dr Khalid Hussain has saved four patients at GOSH from having their pancreases removed through the discovery of a new treatment - an insulin production inhibitor called sirolimus and has recently published his findings in the *New England Journal of Medicine*. For more information on this story, please read the Great Ormond Street Hospital press release.

Parental genes found to be influencing babies' birth weights


Professor Gudrun Moore

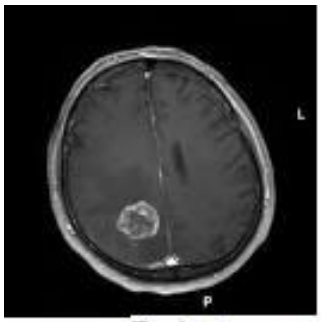
Low birth weight is known to increase future risk of chronic diseases, such as type 2 diabetes and cardiovascular disease. A team of researchers led by Professor Gudrun Moore at UCL ICH has recently linked expression of paternal Insulin-like growth factor 2 (IGF2) to fetal growth in the first trimester of pregnancy. This shows two things: that the father's genes influence the baby's weight at birth; and that there is potential for using IGF2 as a growth biomarker to monitor 'at risk' pregnancies. The study was published in *PLOS One* and more details can be found in the GOSH press release.

New funding secured for investigation of novel therapies for birth defects
We would like to congratulate Professor Nick Greene on receiving a Newlife Foundation award to study disease mechanisms and evaluate therapies for non-ketotic hyperglycinemia. This rare debilitating disease occurs in infants and causes profound neurological impairment and early death. The research will investigate the developmental progression and metabolic basis of this disease and test potential therapeutic approaches.

New findings affecting treatment of neonatal onset epilepsy
The neonatal epileptic encephalopathies are characterised by the onset, soon after birth, of drug-resistant seizures associated with severe neurological dysfunction. They can be fatal and include a seizure disorder, which is caused by a deficiency of pyridox(am)ine 5'-phosphate oxidase (PNPO). This enzyme is involved in the production of the active form of vitamin B6 (pyridoxal 5'-phosphate) which influences brain activity by regulating the production and breakdown of many neurotransmitters in the brain. Professor Peter Clayton and Dr Philippa Mills at ICH have led a collaboration between more than 10 international research centres that have found that this disorder can be treated with pyridoxine, in addition to the conventional treatment, pyridoxal 5'-phosphate (PLP). The group found that stratification of patients into groups allowed for identification of personalised treatment options with either pyridoxine or PLP. These findings are published in Brain supports the use of DNA and biochemical tests for PNPO deficiency in a wide range of infants with epilepsy.

Novel therapies for childhood disease theme news

New study aiming to beat childhood brain tumours


Brain tumour

Brain tumours are the leading cause of death from cancer in childhood. A collaboration between ICH/GOSH, Newcastle University Northern Institute for Cancer Research/Royal Victoria Infirmary and the Institute of Cancer Research/Royal Marsden Hospital is about to embark on a study aiming to improve survival rates amongst children with high-risk tumours. The research teams, including BRC-supported Dr Darren Hargrave, will use novel screening techniques to analyse the genetic make-up of tumours. Findings are hoped to enable fast translation to tailor-made treatments. The study is co-funded from grants from Great Ormond Street Hospital Children's Charity, the Brain Tumour Charity and Children with Cancer UK. A GOSH press release can be accessed for further information.

First approved treatment for Morquio A syndrome
(picture) On 14 February 2014, Vimizim (elosulfase alfa) has received the first ever approval from the U.S. Food and Drug Administration (FDA) as a treatment for Morquio A syndrome. Morquio A syndrome is a rare, autosomal recessive lysosomal storage disease caused by a deficiency in N-acetylgalactosamine-6-sulfate sulfatase (GALNS). The condition causes problems with bone development, growth and mobility. BioMarin sent sincerest thanks to GOSH, its patients and their families for participation in the clinical development and approval of VIMIZIM enabling treatment delivery to many patients. The lead clinicians at GOSH were Drs Ashok Vellodi and Maureen Cleary. GOSH recruited two patients to the trial, altogether the UK contributed 27 patients to the trial and globally 176 patients participated in the trial. Further details are available in the full FDA press release and the BioMarin press release.

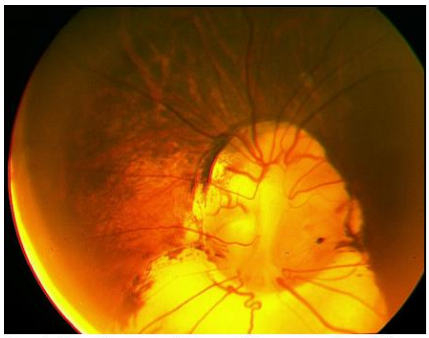
Gene, stem and cellular therapies theme news

GOSH participating in clinical trial investigating a potential new treatment for Childhood Cerebral Adrenoleukodystrophy (CCALD)

Untreated, CCALD is a devastating condition which may progress rapidly leading to a vegetative state and eventually, death. Currently the only effective treatment option is allogeneic haematopoetic stem cell transplant (HSCT). This is a medical procedure in which a patient receives stem cells from a donor who does not have CCALD. GOSH is participating in the Starbeam Study sponsored by bluebird bio, Inc. The aim of this trial is to investigate if delay or prevention of progression of the disease can be

achieved safely and effectively by a lentivirus-based autologous haematopoetic stem cell therapy. In this type of therapy a lentivirus is used to deliver genes into the patients' blood that can induce the production of multipotent haematopoetic stems (blood cells that can give rise to any other blood cells), hence correcting the disease. GOSH has recently completed a follow up evaluation of the first study subject, who received the investigational gene therapy treatment in Boston. This represents a significant milestone for GOSH and the study subject; under the study protocol, the team at GOSH can conduct follow up visits on study subjects. For more detailed information on the condition and current treatment options, please visit this link to our BRC website.

New gene discovered linked to childhood blindness



A coloboma is a gap in part of the structures of the eye caused when a baby's eyes do not develop properly during pregnancy. This image shows a coloboma in the retina at the back of the eye.

Ocular coloboma is a congenital defect causing childhood blindness worldwide. It affects 1 in 10, 000 births. To-date, the genetic basis of the defect is poorly understood. Research led by Professor Jane Sowden of ICH in collaboration with the BRC funded GOSgene facility and GOSH has identified a novel homozygous mutation in a gene called *SALL2*, which is causing ocular coloboma. This is the first report linking *SALL2* mutation to coloboma. This research increases our understanding of the cause of coloboma conditions and will improve genetic diagnosis for children and their families. The study was published in the journal *Human Molecular Genetics*.

Diagnostics and imaging in childhood disease theme news

New study starting to investigate using biomarkers to improve outcomes for patients affected by Wilms tumour

Professor Kathy Pritchard-Jones

Wilms tumour is the most common paediatric kidney cancer, affecting 1 in 10,000 children. The study aims to improve personalised treatment by using biomarkers to increase the accuracy of predicting the risk of relapse and to discover new genes that may cause Wilms tumour. This means that use of conventional treatments, which may cause long term side effects, can be restricted to those children whose tumours benefit the most from more intensive therapy. The study will improve understanding of the biological basis of the highest risk types of renal tumours so that children can be offered new anticancer drugs in the future. This information can then be used to inform personalised treatment plans and lead to better outcomes for patients. Professor Kathy Prichard-Jones is leading this study, funded by Cancer Research UK (CRUK) and Great Ormond Street Hospital Children's Charity. Further information on the study can be found in the CRUK press release.

BRC collaborating with Life study

This year sees the start of recruitment to the Life study directed by Professor Carol Dezateux. The Life Study will be the largest UK-wide birth cohort study aiming to collect data from more than 80,000 babies. It has been designed to support research to understand the interplay between genetic and biological factors and the environment experienced by children (including before birth) and how these factors impact on their development, health and well-being. Professor Neil Sebire, a BRC theme lead, is collaborating with the Life Study to optimise biological sample handling, processing and storage in particular through developing and evaluating protocols from pilot experimental work focussed on the collection of placental samples and their long term storage. These pilot samples will originate from mothers delivering at University College London Hospital. This work will help to ensure the quality of the bio samples collected and stored and their value for future research as the study participants are followed through childhood and into adult life.

PATIENTS AND THE PUBLIC

GOSH BRC Outreach Day
On 24 February 2014, our BRC hosted 50 pupils from the London Academy of Excellence for a day to hear about the ground-breaking research being undertaken at GOSH and ICH, and inspire them to pursue a scientific/medical career. The school has been visited by The Rt Hon Michael Gove prior to their visit to the BRC.

The event was the second one of its nature organised by a team involving BRC theme lead Professor Adrian Thrasher and Clinical Lecturer, Dr Claire Booth. Feedback was positive from both pupils and teachers, who in turn can now go on to inspire other students by sharing their experiences from GOSH.

The pupils spent the day with clinicians, basic scientists and clinical scientists, who delivered a series of short lectures and laboratory tours. Lecture topics included 'What is gene therapy?', 'Fixing broken hearts' and 'Rebuilding bodies'. There were also panel discussions, opportunities to ask questions and careers advice, including interview tips and learning the value of work experience. Panel discussions also provided useful insights for the researchers themselves, as scenarios were presented on for instance whether with advances made possible by next generation sequencing technologies, pupils would want to know, if they have a risk of developing cancer in the next 30 years.

Patient and Public involvement in Research training day
A joint Patient and Public involvement (PPI) paediatric research training day was held on 19 March. Partners were GOSH BRC and Guys and St Thomas' NHS Foundation Trust and King's College London BRC (GSTT BRC). Researchers from GOSH, ICH, the GSTT BRC, and UCL Partners attended the full-day training course, which included speakers from INVOLVE and the Research Design Service London. Smaller break-out groups covered topics such as how to access and involve hard-to-reach young people, how to assess the impact of PPI, and a case study example of PPI from a parent's perspective. It is anticipated that the training day will be repeated in the autumn. Following on from this, the PPI lead for research at GOSH UCL BRC, Erin Walker, gave a seminar about PPI in paediatric research at ICH on 25 March.

PPI consultancy
Individual consultancy on the PPI aspects of your research project can be arranged with Erin Walker. If you are preparing a grant application, or want to implement PPI in a current research project, please email Erin Walker to arrange a meeting.

Update from our Young Persons Advisory Group
April has been a busy month for our Young Persons Advisory Group (YPAG). Members of YPAG have been invited to join the Generation R website editorial board, which decides on the new Generation R website. Generation R is an initiative that involves young people in improving research. The YPAG have also been invited to attend a meeting entitled, 'The young people's involvement in Research Workshop', which is an initiative from the Schools Health and Wellbeing Research Network. The purpose of the meeting is to network with other young people involved in advising on research. Additionally, members of the YPAG took part in the Nuffield Council for bioethics conference to provide input into a project on children and clinical research. Altogether this shows that our YPAG group is increasing its portfolio of projects, not only locally but also nationally. If you are a GOSH or ICH researcher and are interested in investigating how the YPAG can contribute to your research, or you are between 8 and 18 years old and you are interested in joining the group, please e-mail Erin Walker.

For the first time at GOSH, we are holding a research awareness week to coincide with 'International Clinical Trials day' on 20 May. The week will aim to raise research awareness amongst GOSH patients, their families and carers, and GOSH staff.

All week, a wide range of activities including presentations, displays and activities are planned to take place in the Lagoon (GOSH canteen) and GOSH Hospital School. Participants will be

offered the opportunity to 'Have their say about what they think about research', take part in hands on activities, listen to short presentations and ask questions. There will also be posters about the research within the BRC and on the history of research at GOSH. Please find the detailed timetable below and on the BRC website.

EVENTS

13 May 2014, 11.00–17.45
NIHR GOSH UCL Biomedical Research Centre Symposium
Kennedy Lecture Theatre, University College London Institute of Child Health
To view the full programme and register for the event, please visit Eventbrite.

19–23 May 2014
Research Awareness Week
Various locations, all below events take place in the GOSH Lagoon
Research awareness week is aimed at staff, families and patients. There will be opportunity to learn about GOSH/UCL's BRC status and about the research take place across the institutions. Below is a preview of some activities taking place during the week. An overview of all planned activities can be found on the events page of the BRC website.

20 May, 15.00–15.15: *"A day in the life of research"* – the Somers Clinical Research Facility
21 May, 10.00–12.00: Posters showcasing research funded by our BRC
15.00–15.15: *"Ethics and Research"* – Professor Faith Gibson
22 May, 15.00–15.15: *"Involving patients and the public in research"* – Dr Erin Walker
23 May, 15.00–15.15: *"Our research at GOSH"* – Dr Julian Hughes

26 June 2014, 2–4.30pm
Industry engagement workshop
Leolin Price Lecture Theatre, UCL Institute of Child Health

13–14 September 2014
Residential National Paediatric Academic Trainee Weekend
Ashridge Business School

- This weekend will provide an excellent opportunity for 40 academic paediatric trainees to develop their research skills in a weekend course supported by the GOSH UCL BRC.
- The innovative programme includes facilitated interactive work in small groups on grant proposals, the peer review process, ethics review, and presentation skills.
- This will be a great opportunity to network with fellow paediatric trainees and academic leaders in paediatrics.
- Please visit the events page on the BRC website to view the draft programme.
- Acceptance to the weekend will be competitive, please complete the application form and submit to Danielle Wagner by 13 June 2014. Successful delegates will be offered a place on the weekend by 30 June 2014.