

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

A partnership between Great Ormond Street Hospital for Children NHS Foundation Trust and University College
London

BRC NEWSLETTER SEPTEMBER 2013

Welcome to the first edition of the NIHR GOSH UCL BRC Newsletter. It will be our way to keep you up-to-date with news and upcoming events within the BRC.

Following the renewal of National Institute of Health Research (NIHR) BRC funding in 2012, we have spent time investing in and establishing our core BRC funded facilities and research programmes. We will use this newsletter, as well as our redeveloped BRC website (with the involvement of members of the Young Person's Advisory Group at GOSH), to share information and stories about the research and events supported by the BRC taking place across GOSH, UCL Institute of Child Health. Our website address is:

<http://www.gosh.nhs.uk/research-and-innovation/gosh-ucl-biomedical-research-centre/>



*Professor David Goldblatt
Director, NIHR Biomedical Research Centre*

In April 2012, the NIHR awarded GOSH £35m funding, over five years, to ensure that our BRC continues to lead on experimental medicine including the discovery of diagnostics and new treatments for childhood diseases. The BRC award supports the pull through of basic scientific discoveries into 'first in man' studies, or as is sometimes the case, 'first in child' studies. GOSH is the largest recipient of nationally commissioned NHS funding in the country (focussed on rare conditions) and is, thus, a unique resource for collecting relatively large cohorts of rare disease whose care is shared with NHS Trusts all over the country. Our clinicians and researchers have access to cohorts of sufficient size that permit meaningful research and advances. Our BRC's focus is thus on rare diseases and is designed to maximise our clinical resource and encourage broad collaboration to enhance patient benefit nationally.

Our Scientific BRC Board includes:

Professor David Goldblatt - BRC Director

Professor Bobby Gaspar - BRC Deputy Director

Professor Francesco Muntoni - Theme lead: Novel therapies in childhood disease

Professor Phil Beales - Theme lead: Molecular Basis of Childhood Diseases

Professor Adrian Thrasher - Theme lead: Gene, stem and cellular therapies in childhood disease

Professor Neil Sebire - Theme lead: Diagnostics and Imaging in Childhood Disease

Dr William Van't Hoff

Professor Jane Sowden

Dr Maria Bitner-Glindzicz.

Our BRC Manager manager is Julian Hughes, and recently Danielle Wagner has joined him as BRC Co-ordinator. Our research programmes are organised into four BRC themes and the BRC also supports staff working in our Somers Clinical Research Facility.

Molecular basis of childhood diseases

GOSH UCL BRC aims to bring together clinicians and researchers from all disciplines to work towards understanding the molecular causes of childhood diseases, including rapid gene identification in uncharacterised genetic diseases.

Diagnostics and imaging in childhood diseases

GOSH UCL BRC funds research to improve diagnostics for rare diseases and the development of new biomarkers and novel imaging strategies to monitor disease progression and response to experimental therapies.

Gene, stem and cellular therapies

We aim to further develop somatic gene and cellular therapies for immunodeficiency disease and a wide range of rare inherited and acquired disorders.

We congratulate the theme on being awarded two Rare Disease Translational Research Collaboration grants.

Novel therapies for childhood diseases

Through access to some of the largest paediatric cohorts in the UK, we undertake novel 'first in man' studies to develop and deliver novel experimental therapeutic interventions.

Somers Clinical Research Facility

This plays a central role in delivering clinical trials and other experimental medicine research. There are currently over 70 active clinical studies conducted within the CRF. It supports through provision of child friendly day care accommodation and expert support for research into childhood diseases.

I hope you find this Newsletter informative. We welcome any comments and suggestions for topics to cover in future editions.



David Goldblatt
Director, Clinical Research and Development
Director, NIHR Biomedical Research Centre

IN THIS ISSUE

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BRC HIGHLIGHTS AND NEWS

Duchenne Muscular Dystrophy (DMD) gene therapy clinical trial success. With support from GOSH UCL BRC, MRC and Sarepta Therapeutics, the MDEX consortium, led by BRC Theme lead Professor Francesco Muntoni, has designed an early clinical study to obtain critical proof-of-concept data for an antisense oligonucleotide for DMD. GOSH, the Institute of Genetic Medicine and Newcastle Royal Victoria Infirmary carried out a phase I-II clinical trial of this novel therapy in 19 patients, aged between five and 15. Results showed that this stratified therapeutic approach restored missing dystrophin

protein in seven of the 19 children with DMD.

Industry collaborations include:

With Summit Professor Francesco Muntoni is screening for compounds for dystroglycanopathies and validating outcome measures for a clinical trial on DMD.

With GlaxoSmithKline, Professor Francesco Muntoni is conducting global stratified medicine studies in DMD patients.

The Board welcomed [Professor Oscar Della Pasqua](#) to the **BRC Strategy Board**. Oscar will play a key role in advising on industry engagement.

We are advertising for two PhD research studentships

We are offering two three-year full-time PhD research studentships in translational clinical research/experimental medicine starting on or before 1st April 2014. The studentships will be fully supported by the NIHR BRC award. For more information, please visit: <http://www.gosh.nhs.uk/research-and-innovation/gosh-ucl-biomedical-research-centre/brc-news-and-events/>

BRC Industry Engagement workshop: This BRC sponsored event took place on 2nd September 2013 and brought together industry and UCL academics to explore the unique challenges faced during the development of new medicines and therapies. Professor Bobby Gaspar, Industry Lead for our BRC, chaired the event. Participants came from both UCL and GOSH and also included external representatives from industry, MHRA and NIHR. This type of event will take place approximately every four months.

The first speaker, Dr Luca Bolliger from **Recordati / Orphan Europe** talked about the substantial market opportunity for orphan drug development, of the 6,000 or so defined rare diseases, drugs for only 300 exist. Given that patients are at the heart of the market, he invited researchers with such patient cohorts to contact him, as the company is interested to form partnerships to take orphan drug development forward to make a difference to patients' lives. He also mentioned the [Orphan Europe Academy](#), which provides education and training for health professionals in rare disease. For a copy of the full presentation, please click [here](#).

Dr Daniel O'Connor from the **MHRA** talked about the orphan drugs designation application system. He explained that benefits included reduced fees, increased likelihood of external investment, protocol assistance and 10 years of exclusivity. For a copy of the full presentation, please click [here](#).

Dr Chris Williams from **UCL Business** talked about why enterprise, intellectual property and commercialization are important and how to leverage your intellectual property. He stressed how vital it was for a researcher to contact him as soon as possible when an idea has been conceived to arrange a meeting. Chris also gave some examples of support provided by UCLB relating to licensing deals. For a copy of the full presentation, please click [here](#).

Professor Francesco Muntoni from UCL Institute of Child Health gave an insight into his interactions with industry as well as the research he is conducting. He reiterated how important it was to file your patent early to prevent any hold up in bringing benefits to patients later on. For a copy of the full presentation, please click [here](#).

Elevator Pitch: BRC theme lead, Professor Phil Beales chaired this Industry, UCL Academia and Rare Disease 'Elevator Pitch' Workshop on 8th July 2013 at the Wellcome Collection, sponsored by the UCL School of Life and Medical Sciences Knowledge Transfer Board. The attendees welcomed 'the opportunity to network with industry representatives', 'to understand how research into rare diseases can be facilitated by support from pharmaceutical industry' and the creation of a 'forum to exchange ideas across the sectors and facilitate meaningful discussions'. The series of three minute elevator pitches given by UCL researchers to a 'Dragon's Den'-like panel were all well received. The panel awarded best pitch prizes to Dr Petra Disterer, UCL Institute for Liver and Digestive Health and Dr Khalid Hussain, UCL Institute of Child Health. The winner of the audience vote was Professor Edward Tuddenham, UCL Cancer Institute.

A new **prenatal Down's Syndrome screening test** is being developed by researchers supported by the BRC funded GOSomics facility. The assay will be based on the use of mass spectrometry to detect peptides from biomarker proteins. The aim is to create a robust rapid multiplexed assay to improve specificity, reliability and reduce cost. This research is a good example of cross centre collaboration with other BRC funded centres that are providing sample cohorts for evaluation of the assay against current methods. The researchers are also working closely with UCL Business PLC. UCLB have filed a patent on this approach and provided proof of concept funding. Currently they are working with UCLB to identify a suitable industry partner to realise and deliver the benefits of this test into the clinic. For the full story please click [here](#).

Professor Lyn Chitty and researchers on the **RAPID** study team funded by both a NIHR Programme grant as well as the NIHR GOSH UCL BRC are working on developing standards to implement non-invasive prenatal diagnosis (NIPD). This will enable families at high risk of genetic conditions to have access to safer prenatal diagnostic tests by analysing cell free fetal DNA in the mother's blood. This approach makes it possible to offer prenatal diagnosis for certain genetic problems in

high risk families using a simple blood test, thereby avoiding the risks of miscarriage associated with the current methods which require invasive tests.

Seven BRC funded PhD students will begin their studies at GOSH and UCL-ICH in the 2013-14 academic year. Their projects will support translational research being undertaken across both organisations. The BRC will support the development of these trainees through access to NIHR training resources and local training events. Information about other BRC training schemes will be featured in future newsletters. PhD Projects and the lead researchers are shown below.

O-Acetyl GD2 targeted immunotherapy for neuroblastoma and related malignancies (Prof John Anderson/Dr Karin Straathof).

How the Skin Barrier Changes with Age and Disease: A study of Critical Proteins & Metabolites Involved in Skin Barrier Integrity (Dr Kevin Mills).

Cell therapy for congenital retinal dystrophy (Prof Jane Sowden).

Elucidating the mechanisms of thrombembolism and structural arterial disease in children with inflammatory bowel disease supervisors (Dr Mona Bajaj-Elliot/ Dr Fevronia Kiparissi).

Systemic in vivo ADA gene delivery using AAV based vectors and gene editing strategies (Prof Bobby Gaspar).

Understanding and predicting neurological disability in cerebral palsy (CP) using advanced neuroimaging (Dr Chris Clark / Dr Lucinda Carr).

Deep phenotyping of Rare Diseases (Professor Phil Beales).

We have also been awarded five **UCL Impact studentships**, acknowledging funding provided by the BRC for collaborative studentship projects as above.

SPECIAL FEATURES

[Centre for Translational Genomics-GOSgene](#)

In 2010, NIHR BRC funding created the opportunity for the development of GOSgene, to facilitate rapid gene identification in uncharacterised genetic diseases. GOSgene provides an infrastructure and step-by-step guidance for selected projects involving linkage analysis and/or next generation sequencing. GOSgene brings UCL/ICH research expertise to PIs and clinicians working with congenital disorders to enable the discovery of new genes. Our initiative ultimately helps improve diagnostic testing, supports genetic counselling, and will guide further functional analysis aimed at understanding the pathogenesis of disease and improving patients' management or developing novel therapies.

BRC funding for 2012-2017 has allowed GOSgene to increase its capacity and support more projects involving gene identification in rare uncharacterised genetic disorders, and GOSgene is now able to process more samples through its exome sequencing pipeline. This expansion has allowed the enterprise to mature and rebrand as the Centre for Translational Genomics, incorporating the genomics and proteomics expertise from across UCL so that we can become the leading children's centre internationally in functional genomics. The continued success in translation is represented by the successful projects in which we are able to identify the causative gene in the different disorders. Currently, our overall success rate is 50%; very high for a gene discovery programme of this nature. Twenty five projects have been adopted by GOSgene since April 2012, utilising samples from over 200 patients. The majority of these projects will be processed through our exome sequencing pipeline for causative gene identification.

[GOSH UCL BRC Translational Biomarker Discovery Facility – GOSomics](#)

GOSomics was established in October 2012 by BRC theme lead Professor Neil Sebire in collaboration with Dr Kevin Mills of the Biological Mass Spectrometry Unit within UCL Institute of Child Health. GOSomics provides the infrastructure to deliver proteomic analysis for BRC researchers and can support pilot analyses and preliminary data for future grant applications. Using state-of-the-art technology, GOSomics enables proteomic biomarker discovery type experiments in rare childhood diseases. This will aid the design of diagnostic tests and help elucidate the disease mechanisms involved in rare diseases. There are currently 18 projects being run by the facility; seven of which are collaborative with other groups and BRCs at UCL. Current highlights include the development of a new rapid and more specific test for Down's Syndrome and, in close collaboration with our sister hospital the National Hospital for

Neurology, the discovery of potential new biomarkers of neurodegenerative diseases (Alzheimer's, Parkinson's disease and Lewy Body Dementia). The GOSomics board meets monthly assessing new proposals for adoption and funding. Once adopted, proof of principle is achieved and for further development, funding is requested to continue the work.

PATIENTS AND THE PUBLIC

Big Bang event: Our BRC Patient and Public Involvement (PPI) leads Ruth Nightingale and Erin Walker, with the assistance of two GOSH research nurses, supported the Big Bang event at Westminster Kingsway College on 3rd-4th July 2013. The Big Bang is a UK-wide programme led by Engineering UK to promote science and engineering to young people. To promote International Clinical Trials day, a mock 'chocolate clinical trial' was set up and was a great opportunity to educate young people and parents about clinical trial research, and to raise awareness about PPI in research at GOSH. All participants enjoyed the workshop and 64% of participants said they were interested in future PPI work and engaging further in research at GOSH and ICH.

Bloomsbury Festival:

15- 20 October 2013

The GOSH UCL BRC is supporting the Great Ormond Street Hospital research tent at the Bloomsbury Festival on 19th and 20th October. Activities will involve understanding DNA through playdoh and a mock clinical trial with chocolate. For more information please visit above link.

EVENTS

UCL Antisense Oligonucleotide Workshop

23 October 2013

Meeting Room 5, UCL Conference Centre, 188 Tottenham Court Rd

For more information, please visit:

<http://www.crick.ac.uk/news/events/2013/10/23/ucl-antisense-oligonucleotide-workshop/>

NIHR Trainee Meeting:

26 and 27 November 2013

Queens Hotel, Leeds

For further information, please visit: <http://www.nihrtcc.nhs.uk/IEA/Annual%20NIHR%20Trainee%20Meeting>

To register, please visit: <http://www.profbriefings.co.uk/nihrtcc2013>

BRC Talks Series

28 November 2013, 4pm – 5.30pm

UCL- Institute of Child Health

Industry Engagement Workshop

23 January 2014, 2pm – 6pm

UCL- Institute of Child Health

For more event listings see the [School of Life and Medical Sciences webpage](#) and the [UCL Enterprise webpage](#).

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