Welcome to the second edition of our newsletter. This is our way to share with you initiatives that our Biomedical Research Centre (BRC) has supported, news from and successes achieved by our faculty members, often in collaboration with other organisations.

Great Ormond Street Hospital (GOSH) is committed to collaborating with other BRC colleagues and I am pleased to announce continued success with obtaining National Institute for Health Research (NIHR) Translational Research Collaboration (TRC) awards. The following are in addition to the two rare diseases TRC awards for Immunology received by Professors Adrian Thrasher and Lucy Wedderburn featured in our September newsletter. As part of a collaboration led by Professor Tim Barrett from the NIHR/ Wellcome Trust Birmingham Clinical Research Facility, Professor Phil Beales has received two Rare Diseases TRC awards, one on Ciliopathies, Bardet-Biedl Syndrome and Alstrom Syndrome and additional funding for biomarker profiling to advance phenotyping on those conditions. As part of a collaboration led by Professor Michael Hanna at the UCL Hospitals (UCLH) BRC, Professor Francesco Muntoni has been awarded two Rare Disease TRC grants for neuromuscular disease. The total NIHR TRC investment in above collaborations is over £1.2 million.

I would also like to congratulate Professor Lyn Chitty on receiving an additional award of over £250,000 from the NIHR for supplementary work and extension of the RAPID programme to evaluate non-invasive prenatal testing (NIPT) for aneuploidy in the NHS.

On 21 November, GOSH hosted the launch of the first UK Strategy for Rare Diseases. The Rt Hon Lord Earl Howe (Parliamentary Under Secretary of State for Quality) launched the strategy. This followed a visit to GOSH which included meeting Professor Bobby Gaspar (BRC Deputy Director, GOSHCC Professor of Paediatrics and Immunology, Consultant in Paediatric Immunology) and a patient of his with a rare immune deficiency treated with gene therapy, and meeting Professor Phil Beales (BRC theme lead), and his laboratory team studying ciliopathies. The strategy aims to build understanding of rare diseases, support patients and families and boost research to find effective treatments and therapies. The hospital was chosen to host the announcement because of its leading role in the care of children with rare diseases. GOSH runs a large number of nationally commissioned services for rare diseases and with its charity, is building a new Centre for Children’s Rare Disease Research which will play a key role in developing therapies for many disorders for which no treatment or cure currently exists to read more, please click here.

In the last month two of our BRC Faculty were featured in the New Scientist. Professor Bobby Gaspar’s trial of improved SCID gene therapy was a part of an article on how gene therapy has successfully cured five children with non-functioning immune systems (to read more, please click here). Professor Phil Beales was featured as Instant expert 36 on “Human cell tails”. 
We were proud to have a number of our staff nominated for the Health Service Journal (HSJ) in their list of Health’s 50 top innovators in 2013. These include BRC supported Clinical Academic Professors Lyn Chitty and Neil Sebire and GOSH Clinical Academic Dr Allan Goldman. We are also delighted to see the shortlisting of some of our UCLP colleagues and collaborators including Professor Sir Peng Khaw and Professor David Fish. They have been recognised for their innovative approaches making a tangible difference to patients, healthcare colleagues, the healthcare system or wider society. To access the full article, please click here.

I would like to congratulations Professor Lyn Chitty on her recent appointment to Clinical Director of the Clinical Research Network for North Thames.

Engagement with our patient population, local and wider community is key to our BRC. In October, the GOSH/UCL BRC led a number of workshops at the Bloomsbury Festival, which is a festival of art, knowledge, and imagination. This year’s theme was vitality: a journey of discovery for mind, body and imagination. We had close to 700 members of the public visiting the tent, who now know more about the research at GOSH and UCL. Activities included DNA bracelet making, a mock clinical trial using chocolate, and a lab experience learning about immunodeficiency and gene and cell therapy. I would like to thank organisers and volunteers who enabled GOSH’s participation.

David Goldblatt
Director, NIHR Biomedical Research Centre
Director, Clinical Research and Development
Professor of Vaccinology and Immunology

Visit our new website: http://www.gosh.nhs.uk/research-and-innovation/biomedical-research-centre-brc/

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UCL Partner Hospitals participating in Genomics England
GOSH, UCLH and Moorfields Eye Hospital are collaborating to contribute over 600 genomes from our patient populations to this pilot project. The three UCL BRCs are working together to deliver and support UCLPs participation in the Genomics England 100K genome project, for more information on the project, please click here.

Successful collaboration in T cell engineering between GOSH, UCL and King’s College London BRCs
An important collaborative pathway has been established between investigators supported by three BRCs at GOSH, UCL and King’s College London (KCL). Results from a first-in-man study of T cells engineered to express a suicide gene were recently published, confirming the feasibility of the approach. To read the full article in PLOS One, please click here. The study, led by Dr Waseem Qasim at UCL- ICH required production of clinical grade retroviral vector in collaboration with the Rayne Institute, KCL followed by engineering a selection of donor derived T cells in the GOSH gene therapy suite. Please click here for more information.

First human trial of new bone-marrow transplant method
BRC researcher Dr Waseem Qasim has been in the news with a pioneering bone-marrow transplant technique that should help with donor shortages. Dr Qasim explained that “these new approaches should hopefully improve outcomes after mismatched transplantation and pave the way for a number of related therapies”. For the full news story, please click here.

Crucial phase reached for new experimental treatment for neuroblastoma
Clinical grade vector manufacture of a gene therapy product for a new experimental treatment for neuroblastoma has reached a crucial phase and will shortly be delivered to GOSH. This trial will be the first clinical study of genetically modified T cells for the treatment of solid tumours in children in Europe is led by Professor John Anderson, a BRC supported Clinical Academic, and sponsored by the Cancer Research UK Drug Development Office. For more information, please click here (link to text below).

Antiretroviral therapy has potential to achieve good immune function in younger children with HIV
A study published in PLOS Medicine with joint senior authors including Professors Nigel Klein and Robin Callard based at UCL- Institute of Child Health (ICH), indicates that younger children with HIV have good potential for achieving high CD4 counts (a measure of a type of white blood cell that correlates with immune function) in later life provided antiretroviral therapy (ART) is initiated according to current treatment guidelines. However, the research also suggests that the recommended CD4 count thresholds for ART initiation are unlikely to maximise immunological health in children who have never received ART before the age of ten years. Please click here to read the full article in PLOS Medicine.

Non-invasive prenatal testing (NIPT) for Down’s Syndrome on trial at GOSH
Professor Lyn Chitty, a BRC supported Clinical Academic, had extensive media coverage following a press release from the GOSH press office regarding the launch of the NIPT for aneuploidy evaluation in the NHS, including on BBC news on-line and ITV news. For more on Professor Chitty’s research breakthroughs and links to publications, please click here.

Update from the NE Thames Regional Genetics Laboratory based at GOSH
GOSH Children’s Charity funded the purchase of an Illumina HiSeq 2500 system which is being used for a non-invasive prenatal testing validation study and for the development of clinical exome sequencing. The Laboratory has recently published a number of important findings based on the implementation of new clinical diagnostic techniques. For more details on these publications please click here.

Identification of a gene critical for normal hypothalamic development
Professor Mehul Dattani’s group in collaboration with GOSgene, a BRC funded facility, has identified a mutation in a gene known as ARNT2. This gene is associated with a clinical syndrome of microcephaly, hypopituitarism and visual and renal abnormality. The significance of this finding helped identify the role of ARNT2 in the development of the human hypothalamus, as well as providing direct insights into this condition for families with affected children. To read more, please click on this link to article in brain.
GOSH UCL BRC agreement to fund a PhD studentship at the EPSRC Centre for Doctoral Training (CDT) in Medical Imaging

On 22 November 2013, the Minister for Universities and Science, David Willetts MP, announced that UCL was successful in obtaining funding for an EPSRC CDT in Medical Imaging. Professor Andrew Taylor, a BRC supported Clinical Academic, will lead the cardiovascular theme in the CDT. CDTs will support research that connects academic research organisations to key industries and important technologies which will aid innovation and growth. In a joint initiative with other UCL BRCs, GOSH UCL BRC has committed funding to one PhD studentship to be undertaken at the EPSRC CDT in Medical Imaging. The full press release for EPSRC CDTs may be read by clicking here.

Recognition of Professor Neil Sebire’s research investigating infant death

Professor Neil Sebire, a BRC theme lead, in his role as Professor of Paediatric Pathology at GOSH/UCL ICH and in recognition of his research and wider national work investigating infant death has been invited to attend the following prestigious events: Reception with Samantha Cameron at 10 Downing Street on 19 Nov 2013 on behalf of SANDS (Still Birth and Neonatal Death Society Charity); Reception with Louise Ellman MP at the House of Commons on 21 November 2013 on behalf of ARC (Antenatal Results and Choices); Reception with The Duchess of Gloucester at St James’ Place on 3 Dec 2013 on behalf of The Lullaby Trust.

Nuclear medicine course

Dr Lorenzo Biassoni, a BRC partially funded Consultant, since 2006 has been organising the paediatric module of the Nuclear Medicine MSc run by King’s College London. This jointly delivered course is contributing to training the future generation of nuclear medicine professionals. The next paediatric module is planned for 21 and 22 January 2014.

THEME UPDATE

Novel therapies for childhood disease

The Dubowitz Neuromuscular Centre, that is part of this theme, is running a number of natural history studies and clinical trials at various stages of progression. In 2013 one trial has successfully been completed, four trials are ongoing, five have opened to recruitment, a further three are due to open to recruitment in November 2013 and an additional clinical trial is planned to start in January 2014. Approximately 140 patients have been enrolled into these research studies to date. For more information please visit this link. We are also working across UCL partners through a UCL Antisense Oligonucleotide workshop that was hosted by Professor Francesco Muntoni and Dr Juliet Ellis. This workshop on antisense immunity aimed to bring together researchers within UCL Partners. It presented a platform for sharing knowledge and experiences with regards to therapeutic development options and delivery techniques. Over 50 people attended the BRC (GOSH/UCL and UCL Hospitals/ UCL BRCs), Prosensa and UCL Business sponsored event on 23 October 2013.

Diagnostics and Imaging in childhood disease

We continue to collaborate with other BRCs, nine of our current 25 GOSomics projects are collaborations with other BRCs, and include a wide range of paediatric diseases. The recent successful award of a UCL Schools of Life and Medical Sciences (SLMS) equipment bid will increase future capacity within GOSomics. BRC support for Neuroscience imaging has enabled development of a normative database of cerebral blood flow parameters in healthy children accounting for known decreases in cerebral blood flow with age. From this we have demonstrated how this can be used to detect abnormal cerebral perfusion in different vascular territories in children with neurological disease. BRC support for Cardiovascular Imaging has enabled the continued running of our dedicated MRI research scanner, with 1,400 clinical research scans and 400 hours of physics research time per year. We have continued to work on a number of important collaborative projects from assessment of the haemodynamic pulmonary hypertension to the assessment of first ever human use of stem cell therapy in paediatric heart failure. In addition to this, our physics translational research work has allowed us to improve scanning sequences as well as developing fast MR acquisitions. These have been transferred to the clinical setting resulting in greatly reduced scan times for patients.

Molecular basis of childhood disease

At the Centre for Translational Genomics – GOSgene we use next generation sequencing technologies, high-end computing and cutting edge software in an attempt to identify rare disease causing mutations in a range of childhood diseases that span the clinical spectrum. In 2013 we have embarked on projects covering 18 separate diseases, comprising 43 families and over 100 samples. On-going work has identified a number of known disease genes plus a number of potentially novel findings. Recent examples of publications that have arisen through GOSgene collaborations include the identification of mutations in ARMC4 that cause primary ciliary dyskinesia (Onoufriadis A., et al 2013), mutations in ARNT2 that cause a form of hypopituitarism (Webb, EA., et al 2013, also see below news item) and the genetic cause of Lenz-Majewski hyperostotic syndrome (de Souza, S et al. Accepted for publication Nature Genetics). For more information about the activities of GOSgene please visit this link.
Gene, stem and cellular therapies

Gene and Cell Therapy Centre
The Gene and Cell Therapy Centre is a unique focus for innovative medicine which has been the driving force behind the successful treatment of patients with rare diseases by undertaking manufacture of clinical-grade gene and cellular therapy products. Strategically positioned between Great Ormond Street Hospital and UCL- Institute of Child Health, the centre comprises two MHRA-licensed manufacturing units, a core staff of 10 specially trained personnel, including trial regulators, clinical scientists, and quality assurance officers. The activities of the Centre are overseen by a Steering Group drawn from both institutions that is led by Professor Adrian Thrasher, Consultant in Paediatric Immunology and Judith Cope, Chief Pharmacist. Over the last few years it has become clear that these technologies have applications in many disease states. In addition to current clinical trials for four types of inherited immunodeficiency, the centre is participating in trials relating to skin conditions, metabolic conditions, leukaemia, solid tumours and viral infection. Many more trials are in planning stages and there seem few areas of medicine that will not benefit at some stage in the future. Not only has this benefitted patients at GOSH, but the centre has enabled delivery of cell and gene therapies to other centres both locally and internationally. A big reason for the centre’s success is the ability to link high quality research and good clinical practice. There is an open door policy to research ideas with potential clinical application and the centre works closely with investigators to translate this into a medicinal product that can be given as part of a clinical trial or in cases of special need. The centre now receives major core funding from the BRC and is a resource for all investigators at ICH/GOSH interested in trials of cell and gene therapy. Expansion of activity is inevitable, and plans are underway to develop a state-of-the art new facility as part of the proposed Children’s Centre for Rare Diseases Research.

We have recently attracted interest from other centres and biotechs to apply our expertise in manufacturing gene and cell medicinal products to disease states beyond our original remit of treatments for primary immunodeficiency. One example has been the completion of a cell therapy clinical trial involving manufacture of hepatocytes (liver stem cells) for the treatment of metabolic disease. This was done in conjunction with the Belgian Biotech company and Birmingham Children’s Hospital. Another is the recent gene therapy trial for Netherton Syndrome which has recently opened for which we take a skin biopsy, genetically modify the cells, expand them, then transfer back to the patient in order to help correct their defective skin condition. A further seven trials are in planning stages and covering different diseases in addition to six trials already open.
Ordinary children doing extraordinary things
The BRC supported our Young Person’s Advisory Group (YPAG), a joint initiative with our NIHR Medicines for Children Research Network, through funding a short film about children taking part in research. Two versions were made, one featuring children at the CRFs here and at Alder Hey Hospital, Liverpool, and the other based just here at the Somers Clinical Research Facility. The film was shown at the national event Generation R was attended by 150 delegates from the pharmaceutical industry, charities, NIHR, regulators and international delegates. This short film is available to download (click here), to help anyone interested in supporting children taking part in research. We are grateful for the support given by GOSH Children’s Charity in producing this film.

GOSH Participation in the Bloomsbury Festival
The BRC led a research tent for Great Ormond Street Hospital in the Bloomsbury Festival on 19 and 20 October. This festival of arts, knowledge and imagination was used as a platform to engage with the public highlighting that GOSH is a world-renowned institution for research excellence as well as clinical excellence. Close to 700 members of the public visited the GOSH tent with over 90 percent stating that they had had a positive learning experience. Based on the success of this event, we are now planning for next year.

4 Ps in a Pod : Patients, Public, Professionals and Partners: Education event on Patient and Public Involvement (PPI)
This event was led by the Centre for Nursing and Allied Health Professionals Research on 30 October 2013 and brought together practitioners and researchers from a variety of fields. Experiences with PPI were shared and important issues discussed, including the need to involve stakeholders from all backgrounds from the inception of the research idea. For the full programme, please click here. At the event, we launched our strategy on Patient and Public Involvement and Engagement in Research.

EVENTS

9 January 2014, 12 – 2pm
Funding opportunities available via the UCL Translational Research Office
Leolin Price Lecture Theatre, UCL Institute of Child Health

23 January 2014, 2 - 6pm
Industry Engagement Workshop
Leinsky Room, UCL Institute of Child Health
Draft Programme
Professor Simon Heales, Head of Chemical Pathology/Director of Newborn Screening: Developing methods (biomarkers) leading to earlier diagnosis and monitoring of patients with lysosomal storage diseases
Dr Andy Millar, UK Medical Director: Genzyme: Thinking together outside the label on the bottle
Dr Elin Haf Davies, Enabling Research | Empowering Children, The Paediatric Regulation: Understanding regulatory opportunities
Mr Mark Hallsworth, NOCRI: NOCRI – promoting and supporting collaboration with the life-sciences industry.
25 February 2014, 12.30 - 2pm
BRC Seminar Series
Kennedy Lecture Theatre, UCL Institute of Child Health

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