

## Welcome

As 2011 comes to a close, it's been another successful year for the Manchester BRC. From lab-based studies to trials of new therapies, our focus on understanding the genetic basis of conditions, from birth to old age, is successfully delivering results for patients.

Our Academy for Training and Education is going from strength to strength, with fellowships awarded to six young biomedical researchers in October. We continue to equip our fellows with the skills to carry out research relevant to the NHS, and help them work towards gaining external fellowships.

Other highlights include publications by BRC researchers and BRC research groups continuing to attract major funding awards, such as the CADET facility receiving a substantial grant for research into a potential future treatment for diabetes.

A particularly outstanding achievement – highlighted on this page – is the award by the National Institute for Health Research (NIHR) of a Biomedical Research Unit in musculoskeletal research to Manchester. Congratulations to Deborah Symmons and her colleagues, and my added thanks to those who contributed to the application process. However, it is not possible to overlook the fact that NIHR funding for the Manchester BRC was not renewed. Disappointing though this is, it must not detract from all the exciting and important work undertaken by BRC researchers and clinicians since 2008 thanks to NIHR funding.

The arrival of Professor Ian Jacobs as Vice-President and Dean of the Faculty of Medical and Human Sciences represents an excellent opportunity to boost translational research within The University of Manchester, to continue streamlining experimental medicine facilities between the Trust and the University. This will allow a commitment by these partners to allow the Manchester BRC to continue to drive innovation and to translate biomedical research into NHS practice in 2012 and beyond.



**Professor Graeme Black, Director of the Biomedical Research Centre**

## Manchester to host new £5m arthritis research unit

**Patients across the North West and beyond are set to benefit from a new national research unit based in Manchester which will investigate the treatment of arthritis and other diseases affecting the joints and muscles.**

The Manchester NIHR Biomedical Research Unit (BRU) will be run in partnership by Central Manchester University Hospitals NHS Foundation Trust and The University of Manchester. The partners already have a highly regarded Musculoskeletal (MSK) Research Group, and have successfully applied to the National Institute for Health Research for almost £5 million to set up a nationally recognised BRU to extend the group's work.

Led by Professor Deborah Symmons, the team of researchers and clinicians will pioneer new methods of assessing early response to treatment in adults and children with MSK disease, new ways of preventing rheumatoid arthritis and its complications, new therapies for arthritis and new resources for patients to help them achieve the best response to treatment.

"This is a hugely exciting development for Manchester," said Professor Symmons. "Our research theme is, 'Treating arthritis: right first time'. By understanding why some patients respond to certain treatments and others do not, we will be able to ensure that patients get the right treatment for them from the earliest weeks of disease. Indeed, in the case of rheumatoid arthritis, we believe that



**Professor Deborah Symmons**

we will be able to prevent the disease developing in people who are at high risk.

"The benefits for patients are significant: fewer cases of rheumatoid arthritis and its complications, and effective treatments given earlier in the course of disease with fewer side effects leading to better disease outcomes for the most common forms of arthritis."

Mike Deegan, Chief Executive of the Trust, said: "Congratulations to the successful BRU team on an excellent bid and a very welcome result. This further enhances Manchester's already strong reputation for musculoskeletal research, and will significantly boost the work of translating it into innovative treatment for patients."

Professor Ian Jacobs, Vice-President of The University of Manchester and Dean of the Faculty of Medical and Human Sciences, added: "This is important recognition of the quality of musculoskeletal research being conducted by Professor Symmons and the team. It is built upon outstanding collaborative interactions between the University and NHS Trust and most importantly will bring benefits for the quality of life of our patients."

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Genetic solution found to devastating eye disease

# Successful first year for BRC Biobank

**The Biomedical Research Centre opened its Biobank in 2010 and in its first year the team, led by Dr Jay Brown, have banked over 5,000 individual specimens from patients undergoing surgery at Central Manchester University Hospitals.**

By using the dedicated biobanking facility, researchers can save on equipment and staff costs and have confidence that their valuable samples are stored in a secure environment staffed by experienced personnel.

All specimens are obtained ethically and with appropriate consent and the Biobank is licensed by the Human Tissue Authority. With the regulatory requirements taken care of, researchers are free to concentrate their efforts on research.

**“I have been tremendously impressed with the service offered by the Biobank”**

Dr Martin Rutter

A prime example of success can be seen in a study looking at molecular pathways in cardiovascular disease, run collaboratively between the Manchester Diabetes Centre, CADET and the Biobank.

Chief Investigator Dr Martin Rutter said: “I have been tremendously impressed with the service offered by the Biobank. I lead a group developing a complex vascular tissue sampling study which involves the preparation of tissue for RNA, protein and metabolite quantification. The Biobank has helped with the ethics application, and has supported and contributed significantly to the development of the study protocol.

“Their sound understanding of the Human Tissue Act and other important regulations has been invaluable in the setting up of this study. The processing of the vascular tissues, and the general work of the team, is scientifically rigorous, and yet straightforward and practical in its execution, which makes the collection of tissue much easier than one might imagine.



They have been an invaluable resource, and I am sure that our study would have been virtually impossible to initiate and run without their fantastic support.”

The Biobank has set up two collaborative agreements to supply specimens for research in the private sector with Biopta Ltd and Abcellute Tissue Bank.

Jacki Trafford, Procurement Manager at Abcellute Tissue Bank, said: “Using the Biobank allows us to be very confident about the research donation process. It is extremely helpful to have dedicated and trained staff to ensure the potential donor is given all the options regarding research donation, take informed consent and supply us with appropriate anonymous donor information, as well as ensure the samples are packaged and transferred to the dedicated courier.

**“Using the Biobank allows us to be very confident about the research donation process”**

Jacki Trafford,  
Abcellute Tissue Bank

“Knowing that each step of the donation process is monitored and undertaken by Biobank staff also helps us in our reassurances to the researchers we supply with tissue.”

Access to tissues and associated clinical data is open to all researchers in academic institutions, NHS and commercial organisations.

Researchers interested in using biomaterials or services provided by the Biobank can find out more by contacting [Jay.Brown@cmft.nhs.uk](mailto:Jay.Brown@cmft.nhs.uk)

# Genetics 'cloud' to create new opportunities



Professor Carole Goble at The University of Manchester

**Patients across the UK will benefit from a project underway in Manchester and Cambridge to make it much easier to store genetic information and make it available to researchers and clinicians.**

Eagle Genomics Ltd, a leading open-source bioinformatics service provider, is heading a consortium that will investigate cloud computing technology to see if it can be used to safely store the huge amounts of

information produced when individual genes are sequenced and analysed.

Access to this information will enable medical researchers who are developing and testing new treatments to compare large amounts of information and find common genetic links. This technology will also help clinicians to look at an individual patient's genetic make-up to aid diagnosis and ongoing treatment.

The consortium comprises

Eagle Genomics Ltd, The University of Manchester and Cytocell Ltd, with assistance from NGRL, based at the Central Manchester University Hospitals NHS Foundation Trust, and the BRC. The £500,000 project is funded by the UK's national innovation agency, the Technology Strategy Board.

"Cloud computing allows huge amounts of data to be stored and accessed from anywhere, rather than individual hospitals and research

institutions having to buy, house and run enormous servers. Current NHS IT services are not geared up to deal with this kind of specialist requirement," explained Andrew Devereau, the NGRL project lead who is working alongside Professors Carole Goble and Andy Brass from the University.

The project started in August and a fully functional system with an initial selection of analyses should be available by December 2012.

## Manchester gears up for new macular degeneration trial

**A research team at the Manchester Royal Eye Hospital, led by consultant ophthalmologist Mr Tariq Aslam, is expecting to host a second major trial of a new treatment for wet age-related macular degeneration (AMD) later this year.**

In the UK 35,000 new cases of wet AMD are diagnosed each year, with the current treatment limited to a monthly injection into the eye. If left untreated, wet AMD can result in blindness. It mainly occurs in people over the age of 65, and affects 250,000 people in the UK.

In March this year Mr Aslam ran a clinical trial of a new non-invasive device called IRay which uses low voltage radiation, similar to a dental x-ray, to treat wet AMD.

Patients who participated in the trial sat at the IRay machine, with their chin on a chin rest. A contact lens was placed on the surface of their eye to help maintain eye position and tracking. A robot tracked



Mr Tariq Aslam

any eye movement and maintained stability, allowing a controlled dose of radiation to be precisely delivered into the eye.

The device was developed by US-based company Oraya Therapeutics, which chose Manchester to be the first centre in the world to install the newest version of the IRay system in September. The system incorporates enhanced features designed to improve ease of use and to further reduce treatment and procedure time for the patients and clinical staff.

The IRay trials are supported by the National Institute for Health Research Manchester Biomedical Research Centre.



## The Research and Innovation Conference 2011

**Registration is still open for this year's Central Manchester University Hospitals NHS Foundation Trust Research and Innovation Conference, which takes place on 22nd November.**

The keynote speakers will be Professor Dame Nancy Rothwell, President and Vice-Chancellor of The University of Manchester and Professor Rosalind Smyth, Director of the NIHR Medicines for Children Research Network.

Drop in advisory clinics from NIHR Research Design Service for the North West will be available on the day. This is a chance for researchers to gain expert one-to-one advice on research ideas or draft proposals.

The conference will also include talks from Manchester's next generation of leading academics, a Manchester Academic Health Science Centre update and oral and poster presentation competitions.

For more information please email [Brenda.johnson@cmft.nhs.uk](mailto:Brenda.johnson@cmft.nhs.uk)



# Academy for Train

## Congratulations to the six new BRC fellows

As a result of the Biomedical Research Centre's Training Fellowship call earlier this year, the BRC has recently appointed six new clinical research fellows. Each fellow has been awarded one year of funding starting in October 2011. The Clinical Research Fellowships have been awarded to researchers in a number of different research areas including, endocrinology, paediatrics and maternal and fetal health.

**Claire Bonshek** – Early life identification of genetic and metabolomic signatures in primordial growth disorders for use as biomarkers of poor growth potential.

**James McCaffrey** – Epigenetics in childhood steroid sensitive nephrotic syndrome.

**Katherine Martin** – Defining future targets for anti fibrotic therapy in liver fibrosis.

**Sophia Khan** – Prediction of cardiovascular risk in relation to growth, growth factors and metabolic profiles in children of South Asian (Pakistani) and European origin.



Prof Neil Hanley (far right) welcomes the new BRC fellows (L to R) Katherine Martin, James McCaffrey, Lucy Higgins (L to R front) Claire Bonshek, Sophia Khan and Shruti Garg

**Lucy Higgins** – Predicting fetal compromise using novel biomarkers in women perceiving reduced fetal movements.

**Shruti Garg** – The behavioural phenotype in neurofibromatosis type 1 – characterisation and preparation for a treatment trial.

The new fellows will be equipped with the skills needed to carry out research relevant to the NHS and provided with support to maximise their chances of obtaining prestigious external fellowships.

## Trio of Manchester medics win fellowships

Three second-year academic foundation doctors at Central Manchester University Hospitals NHS Foundation Trust have been awarded Academic Clinical Fellowships (ACFs) after successful research placements supported by the BRC.

Matthew Kirkman has a neurosurgery ACF at Imperial College London and Lolita Chan takes up an ACF in gastroenterology in the North West Deanery, with rotations at various hospitals in the region. Cassandra Sobajo remains in Manchester to do her ACF in ophthalmology at Manchester Royal Eye Hospital. When they have all completed their three-year fellowships the next step will be to apply for external training fellowships.

The three doctors opted to include an academic research component as part of their second foundation year. Prof Ian Bruce was the facilitator on this four-month programme, helping the doctors to select areas that matched their research interests.

The doctors were also encouraged to attend the BRC's regular academic teaching meetings, and to take part in BRC Training Academy events and seminars. This gave them the opportunity to mix with fellow researchers at various stages in their careers.

"Only a few ACFs are available nationally each year, and competition for them is very fierce. It's therefore an outstanding achievement for all three of our Manchester candidates to win fellowships," said Ian Bruce. "Our emphasis on doing everything we can to encourage academic training at the Trust and University has really paid off, and these three doctors are a real credit to Manchester."

(L to R) Lolita Chan, Prof Bruce, Cassandra Sobajo and Matthew Kirkman



## Young Investigator Award success

The Children's Tumor Foundation, a US-based charity, has given University of Manchester researcher Dr Miriam Smith a two-year \$100,000 Young Investigator Award (YIA) to fund her work on identifying novel genes responsible for schwannoma and meningioma tumours.

Miriam began working on schwannomatosis in the US in 2007, and joined the Manchester team led by Prof Gareth Evans and Dr Bill Newman in 2009. Her key interest is in understanding how genetic mutations in patients with schwannomas and meningiomas affect the molecular signalling pathways that lead to the development of these tumours, and how this information can be used to develop new treatments for patients.

Miriam's research will use the BRC's next generation sequencing facilities to identify the genetic changes which predispose patients to develop schwannomas and meningiomas. Miriam benefited from a BRC pump-priming award to help with the initial data collection prior to her YIA application.



Schwannomatosis is a form of the genetic disorder neurofibromatosis (NF), and many of the symptoms overlap with NF2. It affects 1 in 40,000 people who develop benign central nervous system tumours and other neurological complications.

"Congratulations to Miriam on her well-deserved award," said Bill Newman. "She is a key member of our team and the award will enable her to focus on identifying the causes of these tumours, helping to pave the way for the development of new drug treatments."

### A warm Wellcome for Gisela!

The Wellcome Trust has awarded a prestigious five-year Career Development Fellowship to Dr Gisela Orozco, a researcher in the Arthritis Research UK Epidemiology Unit based at The University of Manchester.

The aim of Gisela's study is to follow up previous work that found a region on chromosome 6q23 increases the risk of rheumatoid arthritis. Gisela will investigate how changes in the genetic sequence in that region of the genome cause disease.

Gisela joined the Arthritis Research UK Epidemiology Unit in 2008 with funding from a European Marie-Cure Fellowship and subsequently the BRC supported her research.

## Congratulations to award-winning Biomedicine duo

The outstanding research work of Professor Yanick Crow and Tracy Briggs, both from the School of Biomedicine, has won them recognition from their peers in The University of Manchester.

They were named as winners in the Researcher of the Year and Postgraduate Student of the Year categories at the University's 2011 Professional Support Services and Academic Services Distinguished Achievement Awards.

The winners across all nine categories were chosen for their outstanding performances and included teams and individuals who demonstrated professionalism, teamwork, support, openness and continuous improvement.

People were nominated for an award by their colleagues, and all the entries were then assessed by a judging panel.

Yanick joined the BRC in 2008, as Professor of Genetic Medicines at the University. He has particular interests in the complex autoimmune disorder systemic lupus erythematosus and paediatric neurogenetics. Tracy is a clinical research fellow, also working in the field of the genetic causes of autoimmune diseases like lupus.



Professor Yanick Crow



Dr Tracy Briggs

## Upcoming Nowgen training courses

Nowgen, part of the Biomedical Research Centre, specialises in the delivery of professional training in the areas of genetic medicine, molecular biology and bioinformatics.

### 8 December 2011 Personalised medicine study day

This one-day course will focus in particular on the use of personalised medicine (pharmacogenetics) to improve the safety and efficacy of drug treatment in various disease areas as well as the health economic implications. It is an introductory level course that is suitable for delegates within the pharmaceutical industry and healthcare sector.

### 9 December 2011 Biomarkers in research and clinical practice

This new one-day course has been developed as part of Nowgen's Personalised Medicine themed training programme.

Delegates will gain an insight into the discovery of novel biomarkers and there will be open discussion sessions for delegates to talk about their areas of specific interest. This course is aimed at delegates within the pharmaceutical industry and healthcare sector who require an understanding of biomarkers in research, drug development and clinical practice.

If you would like to book onto one of these courses please visit [www.nowgen.org.uk](http://www.nowgen.org.uk)

## New partnership for Human Performance Laboratories

The Wellcome Trust Clinical Research Facility (WTCRF) has recently signed a service level agreement with the University of Salford in relation to the facility's Human Performance Laboratories. The service level agreement will benefit investigators by providing dedicated support and advice for studies with a human performance element.

Salford's School of Health Sciences will ensure that equipment is correctly maintained and calibrated. Training will also be available to all investigators and researchers using the equipment. The School of Health Sciences will also assist in writing research protocols and standard operating procedures where human performance equipment is being used.

Studies already underway at the WTCRF include an exploratory trial to investigate the feasibility of exercise training and physical activity advice to adults with group II and group III congenital heart disease.



## New Arteriograph equipment now available at WTCRF

The Wellcome Trust Clinical Research Facility has recently purchased an Arteriograph to assist with development of studies in four key areas: cardiovascular, dermatology, musculoskeletal and maternal and fetal health.

This new equipment will help the facility's aim of incorporating gold standard Pulse Wave Velocity across the four identified research study areas. Evidence shows that 'aortic pulse wave velocity (aPWV)' is a powerful independent predictor over and above, and often displace, traditional risk factors including blood pressure.

The principle relies on estimating the forward and backward reflection wave from the aortic route to approximately its bifurcation – distance is estimated by a surface measure from the sternal notch to the pubis. Initial results show a good comparison when calibrated against MR imaging.

This recent acquisition is accompanied by an upgrade to the WTCRF's ultrasound facilities, with a Phillips iu22 system being purchased to run alongside the existing Philips HD15000 available to investigators. The new system is available to investigators in both the Adult and Children's Research Facilities.

If you would like to find out more information or are interested in using the new equipment, please contact Ian Mackay, Research Study Manager on **0161 906 7517** or [Ian.Mackay@wtrcf.nhs.uk](mailto:Ian.Mackay@wtrcf.nhs.uk)

## Another global first for the Children's Clinical Research Facility

Following on from the article in the last BRC Bulletin, the Wellcome Trust Children's Clinical Research Facility has secured another global first recruit in a clinical trial, bringing the total to eight. With 16 studies being carried out at the facility to date, a rate of 50% global firsts is a fantastic achievement for the facility and Manchester.

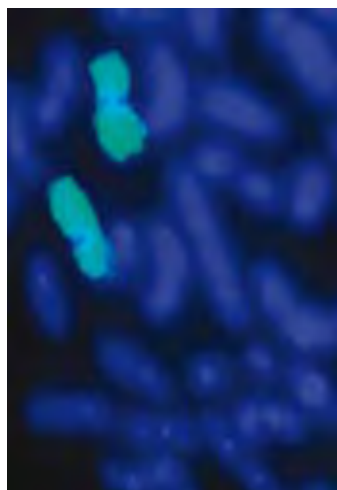


# Genetic medicine team celebrate double funding success

**Professor Yanick Crow and his team are celebrating two major grant awards, one for their work on the pathology of systemic lupus erythematosus, and the other on intracranial calcification in children.**

Working with colleagues at the University of Washington, Seattle, the group will study the pathways linking tartrate resistant acid phosphatase (TRAP), interferon and lupus. Professor Crow is the PI on the project, which has been funded with a grant of \$327,601 from the Alliance for Lupus Research.

Professor Crow's group recently published results in *Nature Genetics* to show that mutations in the gene encoding TRAP predispose



to the development of the complex disorder lupus through dysregulation of type I interferon metabolism. The aim of this new two-year study is to try to

understand how a loss of TRAP activity causes an upregulation of interferon, and how this links to lupus.

Meanwhile, the Great Ormond Street Hospital (GOSH) Children's Charity has awarded £259,000 for a three-year study of the clinical, radiological and molecular definition of paediatric neurological phenotypes associated with intracranial calcification.

The aim of the new study is to provide paediatric neurologists worldwide with a working classification of intracranial calcification at the radiological, clinical and genetic levels.

The GOSH panel making the award stated that the clinical information yielded by grouping patients according to patterns

of intracranial calcification would be of sufficient value to reduce the number of tests they are subjected to, and to provide accurate genetic counselling for families. The research area was considered to be of high priority, and potentially of international importance.

Added Professor Crow: "The GOSH funding application very much depended on the BRC's support for Manchester's next generation sequencing (NGS) provision, in which BRC director Graeme Black has been instrumental. Growing recognition of our NGS capability is a significant advantage to Manchester researchers as bids for funding become increasingly competitive."

## Teenagers get Hands on with DNA

**Nowgen is playing a leading role in the national 'Hands-on DNA' network – a major initiative funded by The Wellcome Trust - which will enable over 6000 school pupils across the UK to analyse their own DNA and investigate genetic variation.**

In the first 'Hands-on DNA' Academy in October, the Nowgen education team trained staff from a network of 15 centres around the UK to deliver a schools workshop originally pioneered by Nowgen. The workshops allow teenagers to learn molecular biology techniques and consider how DNA technologies can be applied in the real world.

The project is a partnership between Nowgen, The Association for Science and Discovery Centres, At-Bristol and the Centre for Life in Newcastle.

DNA workshops continue to be at the heart of Nowgen's innovative schools programme: [www.nowgen.org.uk/EducationandSchools](http://www.nowgen.org.uk/EducationandSchools)

School pupils getting 'Hands-on' with DNA



**"Nowgen is proud to be sharing its expertise with centres around the UK. This network will give thousands more young people the chance to experience the excitement of learning about DNA in the lab."**

Kate Dack, Nowgen's Public Programmes Manager

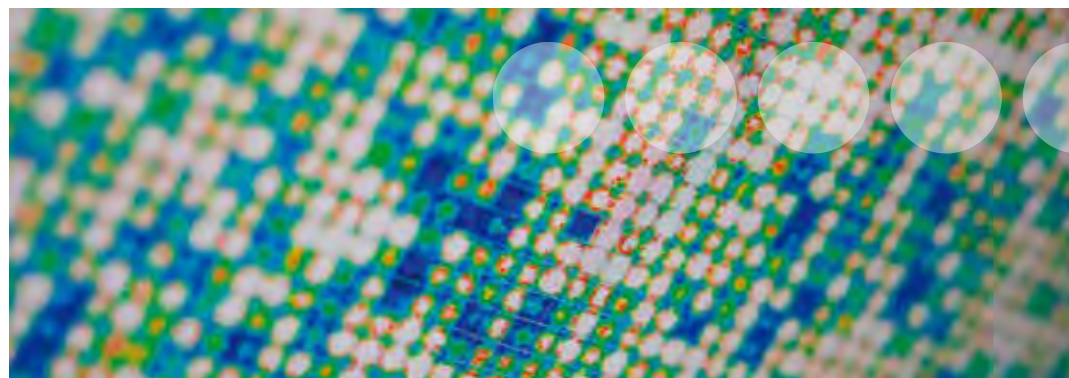
## A Global success for clinical trial recruitment workshop

On Wednesday 5th October, Greater Manchester Comprehensive Local Research Network (GM CLRN) and the Biomedical Research Centre held a workshop for the Manchester research community on the uses of marketing communications in recruitment to clinical trials.

The morning was opened by Professor Ian Jacobs, Vice-President and Dean for the Faculty of Medical and Human Sciences at The University of Manchester, who expressed his support for using new and innovative marketing tools to help boost recruitment to clinical trials in Manchester.

With the support of local radio station Global Radio, the workshop was an interactive morning, with myths around new media such as Twitter addressed and delegates' questions answered.

Speakers included experts from integrated marketing company Cube3, social media expert Alex Butler and the Global Radio team, who have all had experience of working on clinical trial recruitment campaigns. The morning concluded with a presentation on ethics around its importance in the recruitment process.



## Genetic solution found to devastating eye disease

Exome sequencing has helped to identify mutations in the PRDM5 and ZNF469 gene among families with brittle cornea syndrome (BCS). Professor Graeme Black worked with UK and international colleagues to study patients

with BCS, which can cause the corneas to rupture and lead to blindness. Other symptoms include deafness and musculoskeletal problems.

The team clearly established the molecular basis of BCS in the large majority of affected

families. Genetic testing can now be used to help avert the devastating physical and psychological impact of corneal rupture, and to identify carriers of the mutated genes.

*The research results have been published in 'American Journal of Human Genetics'.*

## Nowgen funding success

Last December, in partnership with Dr William Newman, Nowgen ran its first course in stratified medicine, called 'The personalised medicine era and cancer treatment'. The course was well attended a mixture of delegates including NHS workers and pharmaceutical companies, with feedback rating the course as "excellent" and "very valuable".

Due to the success and demand of the course, Nowgen

has developed an expansion of its stratified medicine training programme. As part of this expansion, Nowgen successfully applied for funding from the Lancashire and Cumbria Health and Innovation Cluster (L & C HIEC) to develop introductory

level E-learning sessions in personalised medicine. The project funded by L&C HIEC began in July 2011 in partnership with the NHS National Education and Development Centre, who will be developing the E-learning system.

### DELEGATE COMMENTS

*"Fantastic selection of speakers who portrayed their personal interest in this topic."*

*"A balanced insight into Pharmacogenics."*

*"The meeting was excellent and very valuable."*

## Contact us

For more information about the NIHR Manchester Biomedical Research Centre, or to submit an article for the next edition of this Bulletin, please contact us:

Tel: +44(0) 161 276 3281 Email: [mbrc@cmft.nhs.uk](mailto:mbrc@cmft.nhs.uk) Web: [www.manchesterbrc.org](http://www.manchesterbrc.org)

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