Newcastle University

INSTITUTE OF Genetic Medicine

THE John Walton MUSCULAR DYSTROPHY RESEARCH CENTRE

Celebratory Launch Day

Monday 24th November 2014

The Newcastle upon Tyne Hospitals NHS Foundation Trust

MRC Centre for Neuromuscular Diseases

Monday 24th November

Agenda

09:00	**Registration and refreshments**
09:30	Session 1: *Chaired by Professor Hanns Lochmüller*
11:00	**Coffee Break**
11.20	Session 2: *Chaired by Professor Volker Straub*
12:30	**Lunch & poster viewing**
13.45	Session 3: *Chaired by Dr James Miller*
15:30	**Coffee break**
15.50	Session 4: *Chaired by Professor Katie Bushby*
16:05	Key-note Speech & Official Naming of the Centre
16:25	**Closing Remarks**
16:30	**Drinks Reception with Poster Viewing**
18:00	**Close**

A full agenda is given on pages 14 - 17

Welcome to the John Walton Muscular Dystrophy Research Centre

We are delighted that you are able to join us for the celebratory launch of our new centre. This represents the culmination of 50 years of excellence in muscular dystrophy research and care in Newcastle under a new identity. The new research centre will help us to improve our work at the forefront of cutting-edge endeavours to better understand muscle disease, improving care and treatment of patients around the world.

Over the course of the day, the excellent science of the centre and its distinguished alumni will be presented. We invite you to enjoy the presentations from invited speakers and join us later to view and discuss posters whilst enjoying some refreshments.

We would particularly like to thank our guest speakers, industry sponsors, the colleagues who have organised events today and of course, Lord Walton himself.

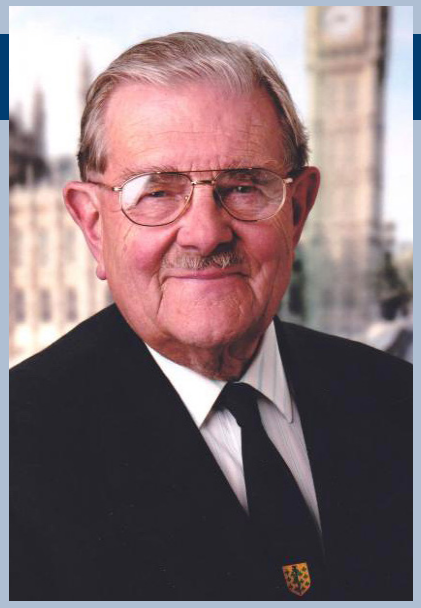
We hope you enjoy the day,
Katie, Hanns and Volker

Lord Walton

Lord Walton's contribution to the field of muscle disease research and patient care is enormous. He has been a leading figure in the field for over 50 years and trained many of the current leaders in the field, represented by our distinguished speakers today.

John Walton's work in the 1950s was a milestone in the classification and description of muscular dystrophies as different entities. His landmark paper with Professor Nattrass in 1954 changed the research and diagnostic landscape for muscle disease.

It was John Walton's pioneering work that saw his department at Newcastle first become recognised as a leader in neuromuscular disorders and established it as the internationally acclaimed centre for muscle disease research that it is today.



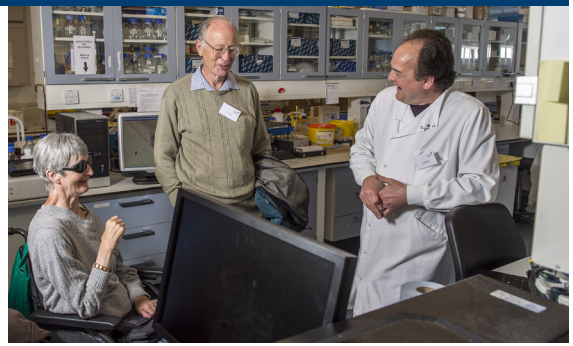
The Lord Walton of Detchant TD

Born locally in Rowlands Gill, John Walton qualified from Newcastle Medical School in 1945, then part of the University of Durham. In 1959 he co-founded the Muscular Dystrophy Campaign of which he is now Honorary Life President. He went on to become both a Consultant Neurologist and Professor of Neurology at Newcastle, and from 1971-1981 was Dean of Medicine at the University.

John Walton was awarded a Life Peerage, becoming Lord Walton of Detchant in 1989.

We are delighted to recognise Lord Walton's contribution to the field in the naming of our research centre and honoured that he is able to join us in the science, discussions and celebrations today.

About the John Walton Muscular Dystrophy Research Centre



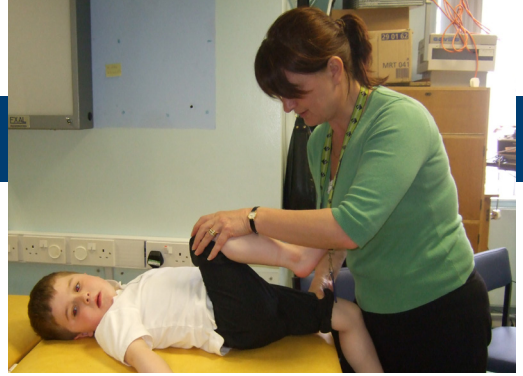
Newcastle has a long history as a centre of international excellence in muscle disease diagnosis, care and research. First established as the Muscular Dystrophy Laboratories at Newcastle General Hospital, the team here has grown over the years and now comprises a group of experts across many fields within muscular dystrophy.
Whilst we are structured around five core areas of clinical care, diagnostics, basic research, clinical research and strategic partnerships and networks it is the significant and important level of collaboration and linkage between these areas that is responsible for the success of the centre as a whole.

One of the great strengths of the centre is its collaborative and multidisciplinary approach, both within the team at Newcastle and with other leading experts around the world. Genetic neuromuscular disease includes some very rare conditions and it is through establishing these partnerships that the biggest strides towards improving diagnosis, care and treatment for patients can be made.

The John Walton Muscular Dystrophy Research Centre team are members of the MRC Centre for Neuromuscular Diseases, a joint enterprise between University College London and Newcastle promoting translational research in neuromuscular diseases. The MRC Centre is a major source of support for activity in Newcastle, including the MRC Centre Biobank and for activities in MRI. It also funds several PhD and clinical students in various disease areas. In addition to this, we have in the past five years trained more than 20 visitors from five continents. Thanks to its extensive international networking, in recent years the centre has also become recognised for its leadership in the rare disease field more broadly and has become part of major global rare disease initiatives including the Global Alliance for Genomics and Health and the International Rare Diseases Research Consortium.

Professors Kate Bushby, Hanns Lochmüller and Volker Straub lead the John Walton Muscular Dystrophy Research Centre and hold joint appointments between Newcastle University and the NHS. With over 115 publications in the last three years, their time is split between research and clinical commitments, both of which focus on neuromuscular disease, and they provide leadership across the five strands of the centre.

Clinical Care



The centre runs multidisciplinary paediatric and adult clinics for **over 2500 NHS patients per year** with a range of neuromuscular diseases throughout the North of England. The research and clinical practice pioneered by the team in Newcastle has contributed to a significant increase in the life expectancy of boys born with Duchenne muscular dystrophy (DMD) as well as the development of internationally recognised care and diagnostic guidelines. Our clinics are directly based on multidisciplinary clinical care for muscular dystrophy as well as the need for this to go hand in hand with research. This approach was first promoted by Lord Walton and his colleagues, including Dr David Gardner Medwin who sadly died earlier in 2014.

Diagnostics

The John Walton Muscular Dystrophy Research Centre leads the National Specialised Commissioning Team (NSCT) service for rare neuromuscular disorders, and is specifically responsible, through the NHS Northern Genetics Service, for the National Limb Girdle Muscular Dystrophy Diagnostic and Advisory Service. We provide diagnostic testing for over 24 different genes known to cause various forms of LGMD. This work, now led by Dr Rita Barresi, is based on pioneering antibody development by Dr Louise Anderson whose antibodies are still the key to diagnosis for many different types of muscular dystrophy. **Over 500 patient samples are received each year.**

Basic Research

The research team conducts basic research into the nature and molecular pathology of neuromuscular diseases using cutting-edge genetic techniques. We identify novel genes, and then assess their function in various model systems – this helps to develop novel ways to treat these conditions. This process is known as translational research, where basic research develops into treatments for patients. Active areas of research include antisense oligonucleotide and gene therapy for DMD, congenital myasthenic syndromes, limb girdle muscular dystrophy and collagen related myopathies.

Clinical Research

The centre plays an active role in clinical research and runs a range of studies with the Clinical Research Facility (CRF) that involve both children and adults with muscular dystrophies. The CRF is a collaboration between Newcastle University and Newcastle upon Tyne Hospitals NHS Foundation Trust. Clinical research, including natural history studies and clinical trials, aims to find new and better ways to treat diseases. We currently have participants recruited into 15 clinical trials or natural history studies in neuromuscular disease. Through registries, biobanks, natural history studies and clinical trials, many patients have the option to participate in clinical research.

Strategic partnerships & networks

The John Walton Muscular Dystrophy Research Centre team has a long tradition of working to establish networks and collaborations with stakeholders from across the neuromuscular landscape, including within the (two-site) MRC Centre for Neuromuscular Diseases. We have active patient and public involvement programmes which include interactions and close working relationships with NHS services as well as many different patient organisations. As well as our role in the MRC Centre, many other networking and collaborative studies are run from the group.

TREAT-NMD Neuromuscular Network

Founded in 2007 and coordinated by Professors Bushby and Straub, TREAT-NMD is a network for the neuromuscular field, now run as the **TREAT-NMD Alliance** and chaired by Visiting Professor Annemieke Aartsma-Rus. The network provides an infrastructure to ensure that the most promising new therapies reach patients as quickly as possible.

The John Walton Muscular Dystrophy Research Centre is experienced in the set-up and coordination of neuromuscular **patient registries**. A number of these are run from the centre, collecting data on over **1,500 neuromuscular patients**. We also coordinate the global registries for DMD and SMA, accounting for over **15,000 genetically confirmed patients**.

Many of the team at the John Walton Muscular Dystrophy Research Centre work in collaborative EU projects. We have had great success in securing funding for such projects over the years and since 2007 have participated in a funded portfolio of projects totalling 73 million EUR putting us firmly at the centre of the European neuromuscular and rare disease community.

A number of major projects are currently coordinated or led by Professors Bushby, Lochmüller and Straub.

RD-Connect

RD-Connect is coordinated by Professor Hanns Lochmüller and is developing an integrated platform connecting databases, registries, biobanks and clinical bioinformatics for rare-disease research.

EUCERD European Union Committee of Experts on Rare Diseases

The EUCERD Joint Action is a healthcare policy project coordinated by Professor Kate Bushby - it supports the European Commission in formulating and implementing healthcare policies pertaining to rare diseases across Europe.

SCOPE-DMD EXON SKIPPING IN DUCHENNE MUSCULAR DYSTROPHY

SCOPE-DMD is coordinated by Professor Volker Straub and will further advance and accelerate the development of PRO045, an exon-skipping compound for DMD. PRO045 is currently in a Phase IIb dose-escalating clinical trial to assess its safety and efficacy.

MYO-MRI is chaired by Professor Volker Straub and will overcome hurdles to the rollout of MR techniques and explore the potential of MRI and MRS as a helpful diagnostic tool and a quantitative outcome measure in NMD clinical trials.

The John Walton Muscular Dystrophy Research Centre also plays significant leadership and research roles in several additional EU projects.

BIOIMAGE-NMD delivers combined structural and molecular imaging biomarkers with proven utility for the detection of therapeutic effects in patients with rare neuromuscular diseases.

NeurOmics is an omics research project which aims to revolutionise diagnostics and develop new treatments for ten major neuromuscular and neurodegenerative diseases.

OPTIMISTIC plans to improve clinical practice and standards of care for patients with DM1 internationally.

Rare Best Practices aims to improve clinical management of rare-disease patients and narrow the existing gap in quality of health care by collecting, evaluating and disseminating best practice recommendations and sharing knowledge globally.

SKIP-NMD is undertaking a safety assessment of a lead PMO compound to skip exon 53, and perform a randomised study looking at safety, biochemical efficacy and exploratory clinical efficacy of this novel antisense in ambulant boys affected by DMD.

All of our projects are supported by active communication and outreach.

www.treat-nmd.eu	@treat_nmd
www.rd-connect.eu	@rdconnect
www.eucerd.eu	@RareDiseasesEU
www.scope-dmd.eu	
www.myo-mri.eu	
www.for-dmd.org	@FOR_DMD
www.bioimage-nmd.eu	
www.rd-neuromics.eu	@rdneuromics
www.optimistic-dm.eu	
www.skip-nmd.eu	

Information about the John Walton Muscular Dystrophy Research Centre can be found at newcastle-muscle.org

Agenda

09:00 *Registration and refreshments (Scotswood suite)*

Session one

Chair: Professor Hanns Lochmüller

09:30 Welcome, Professor Chris Day, Pro-Vice Chancellor for the Faculty of Medical Sciences, Newcastle University

09:40 Opening remarks, Professor Patrick Chinnery, Director of the Institute of Genetic Medicine, Newcastle University

09:50 The Classification, Natural History and Treatment of the Limb Girdle Muscular Dystrophies, Professor Volker Straub, Harold Macmillan Professor of Medicine, Newcastle University

10:20 The Cyanobacterial/BMAA Hypothesis of the Cause of ALS and other Neurodegenerative Diseases, Professor Walter Bradley, Professor and Chairman Emeritus, University of Miami

10:40 Myotonic Dystrophy Type 2 : an Update on Clinical Aspects and Pathomolecular Mechanisms, Professor Giovanni Meola, Professor and Chair of Neurology, University of Milan

11:00 *Coffee break (Scotswood suite)*

Session two

Chair: Professor Volker Straub

11:20 Inherited Defects of Neuromuscular Transmission – How Molecular Findings Result in Better Treatments for Patients with Congenital Myasthenia, Professor Hanns Lochmüller, Professor of Experimental Myology, Newcastle University

11:50 GNE Myopathy Update: Newcastle-Jerusalem Connection, Professor Zohar Argov, Senior Academic Physician, Hadassah University Hospital, Jerusalem

12:10 Deficient RNA Metabolism as a Novel Target in Neuromuscular Disease, Professor Rita Horvath, Professor of Neurogenetics, Newcastle University

12:30 *Lunch & poster viewing (Scotswood suite & mezzanine level)*

Session three

Chair: Dr James Miller

13:45 TTR-Related Amyloid Polyneuropathy: the Experience in an Italian Endemic Area, Professor Giuseppe Vita, Director of Neurology and Neuromuscular Diseases, University of Messina

14:15 Development of Exon Skipping for DMD from Culture Dish to Patients, Professor Annemieke Aartsma-Rus, Visiting Professor from Leiden University Medical Centre

14:40 Looking Forward to New Therapies: the Translational Landscape for Muscular Dystrophies, Professor Kate Bushby, Professor of Neuromuscular Genetics, Newcastle University

15:10 Central Nervous System Regeneration, a Short Retrospective, Professor Albert Aguayo, Emeritus Professor, Former Director, McGill University, Montreal

15:30 *Coffee break (Scotswood suite)*

Session four

Chair: Professor Kate Bushby

15:50 John Walton and the MDC: Founder and Inspiration, Robert Meadowcroft, Chief Executive, Muscular Dystrophy Campaign

16:05 Key-note speech & official naming of the centre, The Lord Walton of Detchant TD

16:25 Closing remarks, Professor Sir John Burn, Professor of Clinical Genetics, Newcastle University

16:30 *Drinks reception with poster viewing (mezzanine level)*

18:00 **Close**

Posters

on display on the mezzanine level

Fatigue and excessive daytime sleepiness in the UK myotonic dystrophy patient registry, A. Atalia

Combining magnetic resonance imaging and histology to investigate the brain in mouse models of Duchenne muscular dystrophy, E. Bagdatlioglu

Patient satisfaction questionnaire, G. Bailey

Preserved expression of truncated telethonin in a patient with LGMD2G, R. Barresi

Intrafamilial heterogeneity in an alpha-dystroglycanopathy due to GDP-mannose pyrophosphorylase B (GMPPB) mutations, M. Bertoli

Deletion of exon 45 is advantageous for survival and maintenance of ambulation in Duchenne muscular dystrophy, C. Bladen

Efficacy of 2nd generation exon-skipping therapy in mdx: cardiac function, in vivo calcium influx and dystrophin restoration, A. Blain

The national diagnostic and advisory service for limb-girdle muscular dystrophies in Newcastle, R. Charlton

Modelling a novel INPP5K mutation associated with Marinesco–Sjögren syndrome in zebrafish, D. Cox

Performance of upper limb scale for DMD: Rasch analysis confirming scale content, M. Eagle

Impact of steroids on Duchenne muscular dystrophy (DMD): a retrospective analysis from the last three decades, M. Eagle

North Star Ambulatory Assessment for dysferlinopathy - scale construction and initial Rasch analysis, M. Eagle

MYO-SEQ: application of next generation sequencing technologies to a large cohort of patients affected by unexplained limb-girdle muscular weakness, M. Ensini

Assessing the potential of a European reference network for neuromuscular diseases: outcomes of an ENMC workshop, T. Evangelista

Manganese enhanced muscle MRI as a sensitive outcome measure of dystrophin restoration in the mdx mouse, E. Greally

Autosomal recessive myofibrillar myopathy caused by ACTA1 mutations, M. Guglieri

Improving the diagnosis of Duchenne muscular dystrophy, M. Guglieri

International clinical outcome study (COS) in dysferlinopathy: results of UK screening questionnaire, E. Harris

Neuromuscular nurse specialistics, L.Hastings

EUCERD Joint Action - working for rare diseases: goals and impact, V. Hedley

Investigating the effect of AGRN mutations on acetylcholine receptor (AChR) clustering in vitro, Y. Issop

The TREAT-NMD Advisory Committee for Therapeutics (TACT): facilitating drug development in rare neuromuscular diseases, L. Johnston

Pathophysiology of anoctaminopathy (LGMD2L), C. Kirk

Strategies for citizen control: patient engagement in rare disease biobank and genomics research in Europe, P. McCormack

The frequency and characterisation of cardiac involvement in female carriers of BMD or DMD: a cross sectional analysis, A. Murphy

John Walton – founder and inspiration, Muscular Dystrophy Campaign

Identification of causal genes in neuromuscular disease by whole exome sequencing, E. O'Connor

A week in the life of a neuromuscular care advisor, E. Perkins

Two founder mutations within GNE gene and high prevalence of GNE myopathy identified in North of Britain, O. Pogoryelova

Engineering and optimisation of mini-dystrophin constructs for Duchenne muscular dystrophy gene therapy, M. Reza

Hypertrophy in mdx and control cardiomyocytes, M. Ritso

UK registry for spinal muscular atrophy, A. Robertson

TREAT-NMD: the global translational research platform for the neuromuscular field, A. Robertson

Improving the diagnosis of Duchenne muscular dystrophy, H. van Ruiten

Research decisions: living with Duchenne muscular dystrophy, S. Skyrme

RD-Connect: an integrated platform connecting registries, biobanks and clinical bioinformatics for rare disease research, R. Thompson

Next generation sequencing in neuromuscular disease: the Newcastle effort, A. Topf

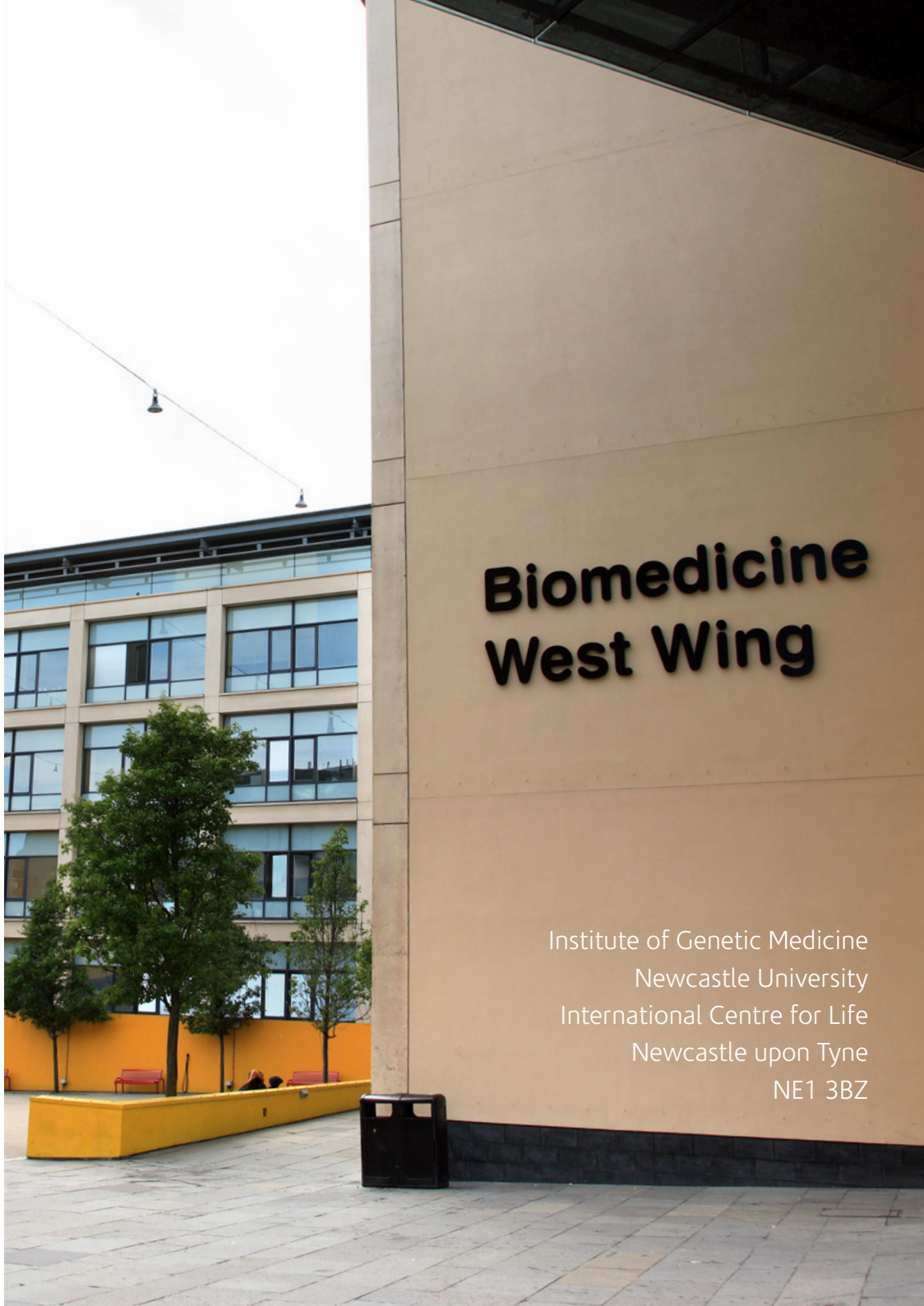
Collagen XII: novel disease causing candidate gene for Bethlem patients, G. Torabi Farsani

NeurOmics: an integrated EU project on omics research for neuromuscular and neurodegenerative disease, C. Turner

Testosterone therapy in DMD, C. Wood

UK registries for facioscapulohumeral dystrophy (FSHD) and myotonic dystrophy (DM), E. Wood

Optimistic: Observational Prolonged Trial In Myotonic dystrophy type 1 to Improve quality of life Standards, a Target Identification Collaboration, E. Wood



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We would like to thank for following organisations for their help and support with this day.

Find out more about the
John Walton Muscular Dystrophy Research Centre
on our website

newcastle-muscle.org