



Queen Square Centre for Neuromuscular Diseases



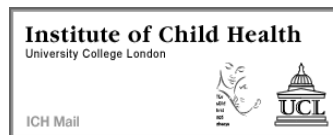
Centre Information

www.cnmd.ac.uk

University College London Hospitals **NHS**
NHS Foundation Trust



Queen Square Centre for Neuromuscular Diseases Partners



**NHS National Commissioning Group
For Highly Specialised Services**



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1. The new Centre for Neuromuscular Diseases, Queen Square - overview and mission

The new Centre for Neuromuscular Diseases at the National Hospital for Neurology and Neurosurgery Queen Square, UCLH-Bloomsbury, is a unique development in UK translational medicine for patients with disabling muscle wasting neuromuscular diseases. The brand new centre facilities which officially opened in December 2009 enables full integration of the highest quality NHS clinical care with cutting edge translational research to benefit patients

Nearly 5000 adult patients with muscle wasting neuromuscular diseases are assessed and treated at the National Hospital Queen Square each year. Many neuromuscular diseases develop in childhood and the Centre works closely with the Victor Dubowitz neuromuscular unit at Great Ormond Street to ensure effective transition to adult care. Neuromuscular diseases include genetic and acquired disorders that often cause major disability and premature death. Examples include muscular dystrophies, myositides, mitochondrial diseases, motor neuron diseases, peripheral neuropathies and disorders of the neuromuscular junction such as myasthenia gravis. Although there have been many important genetic and molecular advances in these diseases there are still hardly any effective treatments that benefit patients. The new Centre combines excellent clinical care, with research and clinical trials aimed at developing new treatments for patients.

The Mission of the Queen Centre for Neuromuscular Diseases:

- Deliver the highest quality patient care and outcomes through cohesive iterative multidisciplinary team working
- Translate research findings into clinical trials and new treatments for NHS patients with neuromuscular diseases
- Act as a national and international centre of excellence for clinical/research training and education in neuromuscular diseases

The new Centre for Neuromuscular Diseases, Queen Square

The key components of the centre which will facilitate excellent clinical care alongside cutting edge translational research include:

- Multidisciplinary clinical teams for diagnosis, treatment and care of patients with all genetic and acquired neuromuscular diseases including myositis, muscular dystrophy, mitochondrial diseases, muscle channelopathies, peripheral neuropathies, myasthenia gravis and motor neuron disease.
- Department of Health nationally commissioning group (NCG) neuromuscular services for patients with muscle channelopathies, McArdle's disease and mitochondrial diseases
- Transition years care and support service in collaboration with GOS Victor Dubowitz unit and centre education/transition pod
- The MRC Centre for translational research in neuromuscular diseases
- The Cochrane neuromuscular unit
- State of the art neuromuscular clinical trials facility

What happens in the Centre for Neuromuscular Diseases?

A fully integrated NHS clinical care and translational research programme is made possible by the co-location of over fifty key staff members including:

- NHS Clinical teams
- MRC Centre research staff
- UCL Institute of Neurology research staff
- Nationally Commissioned NHS teams
- Cochrane unit team
- Active neuromuscular clinical trials unit

Patient centred care for people living with Neuromuscular Diseases

The burden of neuromuscular diseases

Over 70,000 people are living with genetic and acquired neuromuscular diseases in the UK. The prevalence is 1 in 1000 people and therefore in Greater London we estimate there are over 3000 children and 5000 adults affected. These are generally progressive diseases causing major disability and morbidity from a young age. The most severe diseases cause premature death from cardiac and respiratory complications. There is now clear evidence that in order to improve outcomes each patient should have access to a multidisciplinary team of experts lead by a neuromuscular consultant specialist. Furthermore, patients must have a system that ensures easy access to this specialist expertise, since most GPs and DGH doctors and teams will not be familiar with managing neuromuscular diseases. ***Our centre has established such teams for patients and we offer this service not only to patients across London but also throughout the South of England and indeed nationally.***

The populations we serve

In 2009-10 we diagnosed, assessed and treated over 5000 (4000 not including motor neuron disease) adult patients in our centre from virtually every PCT in England. The majority of our patients come from the South of England. Approximately 1800 came from greater London which we estimate is 40% of all adult neuromuscular patients living within the Greater London PCTs. Most of our services are delivered through current PCT based commissioning arrangements, although this is set to change following work we have undertaken in conjunction with the Muscular Dystrophy Campaign. We hope that this work will improve services for patients as these disorders are now included in the so called “national definition set” for specialised commissioning. This means that neuromuscular services can be commissioned on a regional basis with a planning population of 1-5million. Our centre has extensive experience of working effectively with commissioners to benefit patients since we already provide three nationally commissioned services for the whole of England in mitochondrial diseases, muscle channelopathies and McArdle's Disease.

How we support the patient journey

We have developed pathways to help patients from the point of diagnosis through to ongoing regular support, advice, education and management. Diagnosis of neuromuscular diseases is often complex requiring an array of specialised techniques including clinical assessment, muscle and nerve biopsy, genetics, neurophysiology and MRI. Our experience from many patients across the South and England is that diagnosis is often delayed. Delays are in part related to a diminishing availability of true experts in key elements of the diagnostic pathway, most notably neuropathology and muscle and nerve biopsy interpretation. Delayed diagnosis adds to stress and uncertainty for patients and families. ***Importantly, for many of these conditions diagnostic delay contributes to a poor outcome.***

For many patients the journey begins in childhood and transitions to adult life. We have established a unique transition service. We have appointed a consultant who works both at GOS and at the adult centre. *This innovative and unique appointment means that for the last few years before the age of 16 patients can come under the care of the transition consultant and for the years after 16 they can remain under the same consultant.* Transition is not a single hand over clinic but a process for support during a natural period of change into adult life. ***We offer this transition service to all patients with nm diseases currently attending GOS whatever their PCT of origin.*** The dedicated neuromuscular teams including the transition service are outlined later in this brochure.

How we work with the NHS, patients organisations and patients to deliver improved patient outcomes

As a joint MDC Centre of excellence the Queen Square adult centre and the Victor Dubowitz GOS centre have a long track record of working closely with the MDC to improve care for patients and to develop new treatments through research. We recognize the critical importance of measuring the quality of what we do and improving outcomes for our patients. We apply established guidelines to our specialist clinics, and where guidelines are not fully established, we are taking a leading role in their development through national professional organisations that members from our centre lead eg the British Myology Society (Chairman Prof Hanna) and the British Peripheral Nerve Society (President Prof Reilly). We iteratively apply quality measures to all aspect of our services in the three key domains of patient experience, patient safety and patient outcomes. We have worked with the MDC over recent years including giving evidence at the recent all party parliamentary review culminating in the Walton report for neuromuscular services.

Working in partnership with patients and local services

Patient choice is an important and central attribute of the new NHS. We continue to strive to make our services available to all patients who wish to access it. We hold biannual patient days for all neuromuscular patients and their families to offer support, guidance and education. We are also pleased to work with other providers to guide improved outcomes for all patients. We already have an established network of partner hospitals to which NHNN supplies linked consultant neurologists and we provide rapid access to our services through these appointments. The NHNN linked hospitals network spans West to East London and includes Northwick Park, Watford hospital, Royal Free, The Whittington, the Homerton and Whipps Cross. We continue to develop these cross-Trust and cross-PCT boundary links to improve outputs for all neuromuscular patients. We consider there are major opportunities for patient outcomes through a pan-London managed nm network.

UCL Partners and HIEC

UCL partners is an established Academic Health Science Centre that links a world class university, UCL, with major London teaching hospital Trusts including UCLH, Royal Free, GOSH and Moorfields. We have already taken full advantage of this partnership to improve outcomes for patients with neuromuscular diseases through ever closer joint clinical working with GOS and the Royal Free and through education and world class research. We are now pursuing a major opportunity to improve the outcomes for neuromuscular patients in East London working in conjunction with the HIEC initiative (health innovation and education cluster). HIEC links primary care providers with UCLP in order to establish a network to enable clinical excellence to be delivered locally throughout East London and Essex.

Health Intelligence

We recognize the essential need to develop specific data monitoring systems and registries to monitor care and outcomes of all patients with neuromuscular diseases. We have an established cross-trust database between the adult centre at Queen Square and the GOS Victor Dubowitz unit. We would like to extend this across London and potentially the South of England. We are already working with the MDC and have developed the national research neuromuscular research database to enable patients to have more access to clinical trials.

2. Clinical Services

Muscle clinical team and services

Muscle service team

Consultants

Professor Michael Hanna

Dr Matt Parton

Dr Chris Turner

Dr Shamima Rahman

Professor Tony Schapira

Dr Ros Quinlivan joint NHNN–GOS appointment for Transition

Dr Janice Holton- muscle pathology

Dr Nick Hirsch- Respiratory-Neuromuscular intensive care

Dr Perry Elliot-Neuromuscular cardiology service

Dr Doreen Fiahlo-Neurophysiology

Prof Koltzenburg-Neurophysiology

Clinical Nurse Specialist

Catherine Parry

Clinical Support Nurse

Georgie Mewing

Physiotherapist

Liz Dewar

Office Manager & NCG Mitochondrial and Channel Coordinator

Vina Pswarayi

PA to Professor Hanna

Anne Grayson

Secretary to Dr Parton

Marcia Forde

Secretary to Dr Turner

Penny Schafer

Muscle Clinical Research Fellows

Dr James Burge

Dr Robert Pitceathly

Dr Adrian Miller

Dr Dipa Raja Rayan

Dr Jasper Morrow (joint with nerve)

Typical referral pathway for specialist muscle disease specific clinics

Professor Michael G Hanna, Dr Matt Parton, Dr Shamima Rahman, Dr Chris Turner, Dr R Quinlivan, and Georgie Mewing and Cath Parry Clinical Nurse Specialists

Referrals to the specialist muscle service are accepted from any part of the United Kingdom with either a standard referral letter or completed NCG pro-forma for either of the UK national NCG supported services in Muscle ion channel and Mitochondrial disease



Following receipt of referral, an appointment will be made via the hospitals partial bookings team and a letter confirming the appointment will be sent to the patient



For the first consultation the patient will be seen in our unselected referral Specialist Muscle Clinic (URSMC) for an initial assessment by Prof Hanna, Dr Parton, Dr Turner, Georgie Mewing and Cath Parry (CNS)



The URSMC does provide a “one stop” appointment for clinical assessment neurophysiology, genetic testing, genetic counselling and routine blood tests



If further investigations such as MRI, muscle biopsy and lumbar puncture are required, an admission to our investigation day case unit will be arranged



Follow-up for review of selected investigations, diagnosis and treatment initiation will be in our URSMC



Ongoing care:

1. Follow-up in one of the Specialist Muscle Multidisciplinary Disease Specific Clinics
2. Follow-up in the URSMC
3. Local follow-up

**Specialist Muscle Multidisciplinary Disease Specific Clinics**

1. National Muscle ion channel clinic supported by NCG
2. National Mitochondrial disease clinic supported by NCG
3. Myotonic Dystrophy clinic
4. Inflammatory disease muscle clinic
5. Inclusion body myopathy clinic
6. Early adulthood transition clinic
7. DMD adult clinic
8. Neuromuscular Respiratory support service clinic
9. Cardiac neuromuscular clinic
10. Nurse-led immunosuppression treatment clinic
11. Nurse lead telephone advice service and clinics

Day case, 5 and 7 day inpatient service

Diagnostic investigations and intravenous treatments for adult muscle patients are provided in the National Hospital Queen Square. This is most commonly provided within the Day Care Unit in the National Hospital for Neurology and Neurosurgery with the patients going home each evening or being put up by the hospital in a local hotel. For those with more severe mobility problems they are admitted to either the five or seven day unit in hospital for this type of treatment.

This specialised muscle service also offers an inpatient service for those patients who require more detailed investigations including muscle biopsies, lumbar puncture and specialised scanning, and more complex treatment. This is particularly used by other neurological centres around the country requiring tertiary or quaternary opinions. As well as offering a muscle biopsy service we also offer a service to give a second opinion on muscle biopsies done elsewhere nationally.

Nationally commissioned neuromuscular services in the Centre for Neuromuscular Diseases

Three nationally commissioned clinical services are provided from the Centre for Neuromuscular Diseases and are lead by Professor Hanna and Dr Qunlivan

The Queen Square National Specialist Service for Mitochondrial Diseases Prof Hanna [established in 2007] works closely with centres in Oxford and Newcastle to provide the national comprehensive specialist clinical and diagnostic service for patients with complex mitochondrial diseases. The service includes clinical assessment and comprehensive diagnostic work up including genetics, muscle biopsy and biochemistry.

The Queen Square National Diagnostic service for muscle channelopathies Prof Hanna [established in 2001] provides a national clinical and diagnostic service for patients with muscle channelopathies and includes clinical assessment allied to specialist electrophysiology and genetic evaluation. This service is part of the consortium for the diagnosis of rare neuromuscular diseases in collaboration with colleagues in the Dubowitz Neuromuscular Unit GOS, Oxford and Newcastle.

The Queen Square Great Ormond Street McArdle NCG Dr Quinlivan
This brand new NCG service commences in 2011 and provides a unique diagnostic, advisory and treatment service for any patient in England with this metabolic muscle disease.

Peripheral Nerve service team and service

Consultants

Professor Mary Reilly
Dr Hadi Manji
Dr Michael Lunn
Dr Lionel Ginsberg
Professor Henry Houlden
Dr Julian Blake-neurophysiology

Clinical Nurse Specialist

Karen Bull

Physiotherapists

Liz Dewar
Gita Ramdharry

PA to Professor Reilly

Carol Brown

Secretary to Professor Reilly

Michelle Bovell

Secretary to Dr Manji and Dr Lunn

Stephanie Grisdale

Clinical Research Fellows

Dr Elspeth Hutton
Dr Matilde Laurá
Dr Sinead Murphy
Dr Jasper Morrow (joint with muscle)
Dr Alex Rossor

Peripheral nerve clinical service in the centre for neuromuscular diseases

The Peripheral Nerve Service in the Centre for Neuromuscular Diseases offers a comprehensive service for all peripheral nerve diseases. The Service is led by Professor Mary Reilly and the senior members are two other consultants, Dr Hadi Manji and Dr Mike Lunn, one clinical nurse specialist, Karen Bull and one neuromuscular physiotherapist, Liz Dewar. Dr Ginsberg provides specialist peripheral nerve clinics at the Royal Free Hospital.

Specialist peripheral nerve multidisciplinary clinics available

The Peripheral Nerve Service offers a range of peripheral nerve clinics as listed below:

1. General peripheral nerve clinic
2. Genetic peripheral nerve clinic
3. Inflammatory neuropathy/immunosuppression peripheral nerve clinic
4. HIV neuropathy clinic
5. Nurse-led immunosuppression treatment clinic
6. Nurse-led genetic counselling clinic
7. Specialist orthotic and rehab neuromuscular clinic.
8. There are also three nurse-led telephone clinics weekly, dealing with all peripheral nerve problems, but particularly immunosuppression

Mechanism of Referral

Referrals to the specialist peripheral nerve service are accepted from any part of the United Kingdom either as tertiary referrals from other consultants or as second referrals from GPs. Referrals are booked into the appropriate clinic. Most referrals are seen in the general peripheral nerve clinic except for specialised referrals to Professor Reilly's genetic clinic which are directly booked into the genetic clinic. In all peripheral nerve clinics, all new patients are seen by consultants.

All the follow up patients are also seen by consultants but some of these may be seen by Specialist Registrars initially. This is in keeping with our motto of delivering a consultant-led service.

Description of typical clinic attendance for patients

All patients are pre-warned that clinic may take up to half a day. All patients are seen and examined and have either neurophysiology done in the clinic or go to the neurophysiology department for the neurophysiology to be done. In some of the clinics, including Professor Reilly's Thursday general peripheral nerve and Thursday genetic clinic neurophysiological assessment in clinic is done by Dr Julian Blake who has a particular interest in neuropathies.

During the clinic appointment, patients are offered as is necessary a session with the neuromuscular specialist nurse, Karen Bull, and/or a session with the neuromuscular physiotherapist, Liz Dewar.

At the end of the clinic the patient is again seen by the consultant to go over all of the results from clinic and to plan further investigations or treatments.

Copies of all clinic letters from clinic are sent to the patient.

Day case, 5 and 7 day inpatient service

Many peripheral nerve patients who have an inflammatory neuropathy require frequent infusions of immunomodulatory treatments including intravenous immunoglobulin and Cyclophosphamide. This is most commonly provided within the Day Care Unit in the National Hospital for Neurology and Neurosurgery with the patients going home each evening or being put up by the hospital in a local hotel. For those with more severe mobility problems they are admitted to either the five or seven day unit in hospital for this type of treatment.

This specialised peripheral nerve service also offers an inpatient service for those patients who require more detailed investigations including nerve biopsies, lumbar puncture and specialised scanning, and more complex treatment. This is particularly used by other neurological centres around the country requiring tertiary or quaternary opinions. As well as offering a peripheral nerve biopsy service by which we mean we do the biopsies and read the biopsies we also offer a service to give a second opinion on nerve biopsies done elsewhere nationally and routinely request the nerve biopsies of any patient referred to us for a second opinion who has already had a nerve biopsy so that we can review them ourselves.

Ongoing Care

Following a patient's appointment in clinic or an inpatient episode a decision is made that they will either followed up in one of the specialist peripheral

nerve multidisciplinary disease specific clinics or the general peripheral nerve clinic, the nurse led clinics, the nurse led telephone clinics or have local follow up with either the referring physician or general practitioner.

Motor Neuron / Myasthenia clinical services

Consultants

Professor Dimitri Kullmann- myasthenia
Dr Robin Howard-myasthenia and motor neuron disease
Dr Katie Sidle- motor neuron disease
Dr Richard Orrell- motor neuron disease
Dr Nick Hirsch- respiratory support service

Clinical Nurse Specialists

Jan Clarke
Natalie James
Helen Eddlestone

PA to Dr Howard

Sarah Mazdon

Clinical Research Fellow

Dr Jennifer Spillane - John Newson-Davis Myasthenia Fellow

Motor neuron disease service

The NHNN is the MND Association regional care centre for patients with MND and the clinical team are responsible for all aspects of the care of patients with MND in the weekly MND clinic.

Myasthenia Gravis service

A comprehensive outpatient and inpatient service is provided. This includes access to ventilatory support and state of the art neurological medical intensive care facility at Queen Square.

NHS Clinical activities supported by the Centre

Mondays

08:00 – 09:00	Peripheral nerve neuropathology meeting Prof Reilly/Dr Lunn/ Dr Manji <i>Seminar Room</i>
13:00 – 14:00	Peripheral nerve pre-clinic meeting Prof Reilly/Karen Bull/Clinical Research Fellows <i>Seminar Room</i>
14:00 – 15:00	NCG genetics/biochemistry meeting Dr Rahman/Prof Hanna/Dr Heales Seminar Room
14:00 – 17:00	Myasthenia Clinic Prof Kullmann <i>Basil Samuel OPD</i>
14:00 – 17:00	Immunosuppression and complex peripheral nerve clinic Dr Lunn <i>Basil Samuel OPD</i>

Tuesdays

08:00 – 09:00	Neuromuscular journal club Prof Reilly <i>Seminar Room</i>
09:00	Peripheral nerve general neuropathy clinic Prof Reilly <i>Basil Samuel OPD</i>
09:45	Neuromuscular Radiology meeting Prof Hanna
10:15	Muscle ward round Prof Hanna/Dr Parton/Dr Turner

11.30	Muscle pathology meeting Prof Hanna/Dr Parton/Dr Turner/Dr Holton <i>Seminar room</i>
13:30	Muscle clinic and NCG channelopathy clinic Prof Hanna/Dr Turner/Dr Parton Catherine Parry/Georgie Mewing/Liz Dewar <i>33 Queen Square OPD</i>
13:30	Peripheral nerve/general neurology clinic Dr Lunn <i>Basil Samuel OPD</i>
14:00	Respiratory support clinic Dr Hirsch <i>Basil Samuel OPD</i>
PM	Peripheral nerve CNS-led telephone clinic Karen Bull

Alternate weeks

14:00	Muscle clinic Prof Schapira <i>Basil Samuel OPD</i>
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Monthly

16:30	MRC Centre invited speaker trainee tutorial <i>Seminar room</i>
17:30	MRC Centre invited seminar <i>33 Queen Square lecture theatre</i>

Alternate Months

14:00	Joint inflammatory muscle disease clinic Prof Hanna/Prof Schapira/Prof Isenberg <i>Basil Samuel OPD</i>
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Wednesdays

09:00 – 13:00

Teaching ward round
Prof Reilly
Basil Samuel OPD

09:00 – 13:00

Peripheral nerve CNS-led telephone clinic
Karen Bull

Monthly

09:00

IBM clinic
Prof Hanna/Dr Parton
33 Queen Square OPD

Thursdays

09:00

Muscle clinic
Dr Parton
Basil Samuel OPD

09:00

General peripheral nerve/genetic (alternate weeks)
Prof Reilly
Basil Samuel OPD

09:00

General peripheral nerve clinic
Dr Lunn

09:00

General peripheral nerve clinic
Dr Manji

09:00

Motor neuron disease and myasthenia clinics
Dr Howard/Dr Sidle/Dr Orrell/Natalie James

12.30

Muscle team MDT
Seminar room

14:00

NCG mitochondrial clinic
Prof Hanna/Dr Rahman
RLHH

14:00	Myotonic dystrophy clinic Dr Turner
14:00	Peripheral nerve/pain clinic Prof Koltzenburg <i>Basil Samuel OPD</i>
14:00	Gower's Grand Round (Neuromuscular round 4 times per year) <i>Wolfson Lecture Theatre</i>
17:00	Peripheral nerve CPC
Monthly PM	Transition muscle clinic Prof Hanna/Prof Muntoni/Dr Manzur/Dr Robb GOS
Fridays	Research and trials Clinical trials room
14:00	Ward round Prof Reilly
Monthly 15:30	Joint ION/GOS neuromuscular MRI meeting Prof Yousry/Dr Rosendahl Radiology seminar rooms, 8-11 QS/GOS

3. Research activities in the Centre

The MRC Centre for Neuromuscular diseases is one of the MRC's translational research centres and opened in 2008. It is directed by Professor Hanna and is a partnership between the UCL Institutes of Neurology and Child Health, and the University of Newcastle upon Tyne.

Main programmes of research

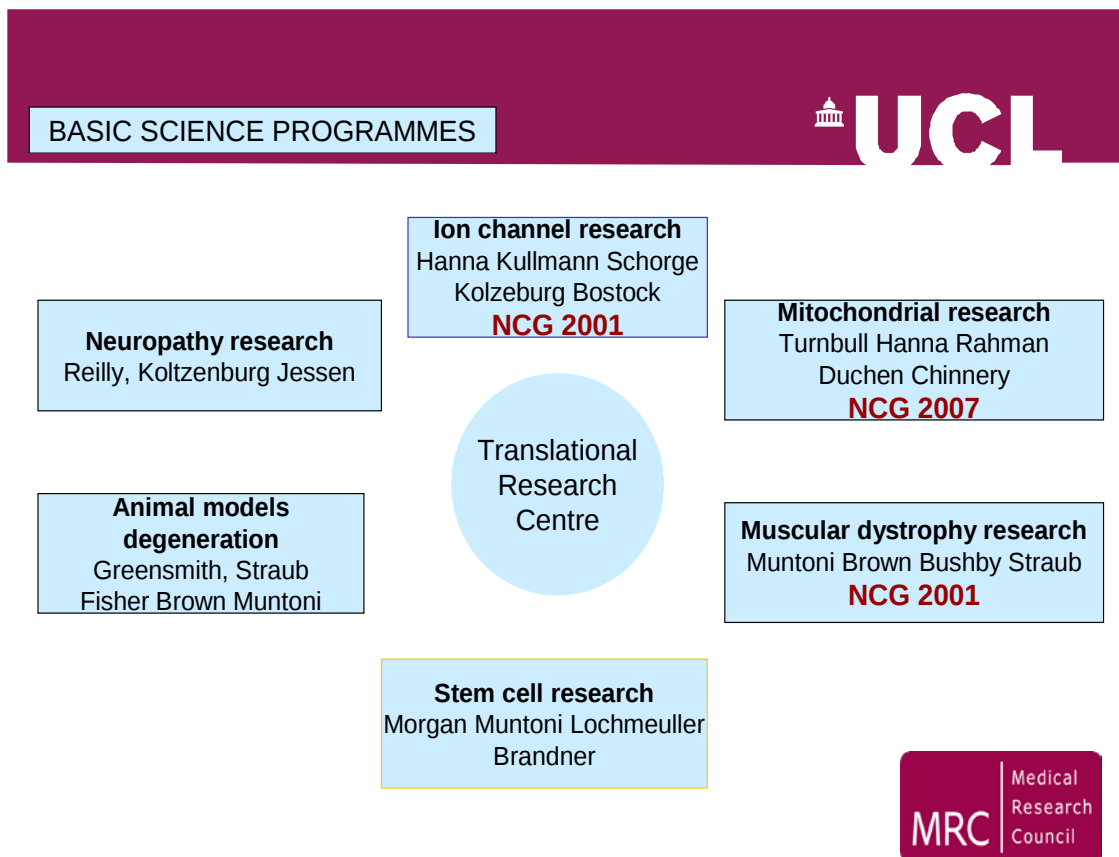
The main programmes of research within the centre have built on existing funded themes currently attracting in excess of £20m of grant income across PI groups in UCL and Newcastle, and have developed new cross cutting collaborations which have capitalized on the recruitment of world class senior academic personnel to UCL and Newcastle.

The main programmes of basic research across the MRC Centre cover major diseases of muscle and nerve

- Molecular mechanisms in muscular dystrophy [Brown, Duchen, Holden, Muntoni, Sewry]
- Mitochondrial DNA neuromuscular disease [Duchen, Hanna]
- Ion channel neuromuscular disease [Hanna, Koltzenburg, Tan, Bostock, Kullmann]
- Muscle stem cell biology [Morgan, Muntoni]
- Genetic neuropathies [Brandner, Fisher, Greensmith, Houlden, Jessen, Reilly]
- Spinal muscular atrophy [Duchen, Fisher, Greensmith, Muntoni]
- Generation of neuromuscular disease mutant mice [Brown, Fisher]
- MRI of nerve and muscles in animals and humans [Hanna, Koltzenburg, Muntoni, Reilly, Yousry]
- Trials & outcomes in neuromuscular disease [Hanna, Muntoni, Reilly, Thompson]

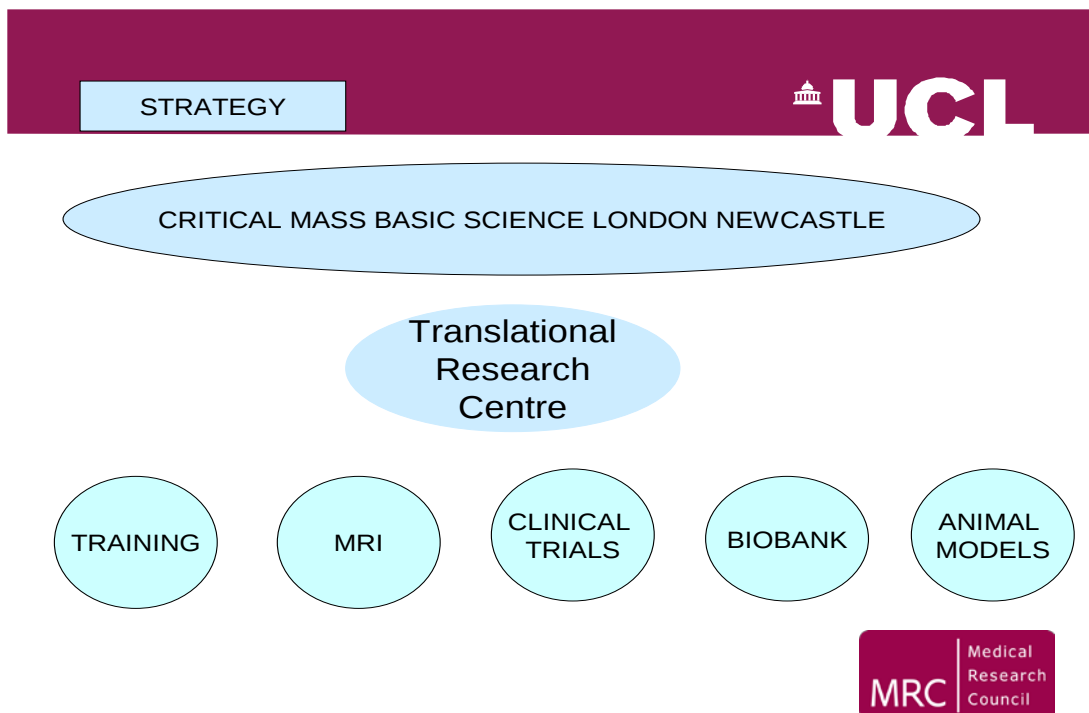
Key science programmes and representative investigators.

NCG-National Commissioning Group-refers to NHS funded national diagnostic and advisory services run by MRC Centre PI's for muscle channelopathies (London-Hanna), mitochondrial disease (joint: Newcastle-Turnbull and London-Hanna joint), congenital muscular dystrophies (London- Muntoni) and Limb-girdle dystrophies (Newcastle-Bushby)



All the main programmes of basic research impact upon and benefit from the following five key areas that have been newly developed in the centre (the underdevelopment of these key areas is a current “block” to effective UK translational research in neuromuscular disease).

- The MRC Centre is initiating and running new clinical trials and is developing a range of specific clinical assessment tools to facilitate future clinical trials in neuromuscular disease in the UK
- The MRC Centre is establishing new cutting edge MRI of nerve and muscle disease in animals and humans
- The MRC Centre is establishing a unique UK biobank of human neuromuscular patients tissues and cells
- The MRC Centre is establishing a network and resource for elucidating the pathogenesis of neuromuscular conditions in mutant mice
- The MRC Centre is attracting and training a new generation of basic and clinical neuromuscular scientists to build future “capacity” in the UK



MRC Centre for translational research in neuromuscular diseases - staff list

Centre Director

Professor Michael G Hanna

Centre Deputy Director London

Professor Martin Koltzenburg

Professor Francesco Muntoni

Centre Deputy Director Newcastle

Professor Kate D Bushby

Centre Steering Committee

Professor Michael G Hanna

Professor Francesco Muntoni

Professor Martin Koltzenburg

Professor Mary Reilly

Professor Dimitri Kullmann

Professor Tarek Yousry

Professor Kate Bushby

Professor Doug Turnbull

Centre Principal Investigators-London

Professor Sebastian Brandner

Dr Sue Brown

Professor Michael Duchen

Professor Elizabeth Fisher

Professor Linda Greensmith

Professor John Hardy

Professor David Isenberg

Professor Kristjan Jessen

Professor Martin Koltzenburg

Professor Dimitri Kullmann

Dr Jenny Morgan

Professor Francesco Muntoni

Professor Mary Reilly

Professor Anthony Schapira

Professor Alan Thompson

Professor Nicholas Wood

Professor Tarek Yousry

Centre Principal Investigators-Newcastle

Professor Patrick Chinnery

Dr Elaine McColl

Professor Hanns Lochmüller

Professor Volker Straub

Professor Douglass Turnbull

Professor Kate Bushby

London Full time staff appointed following commencement of the centre

Non-clinical translational PhD studentships - four years each

Mhoriam Ahmed
Alex Clark
Amy Innes
Phil McGoldrick
Alice Neal

Non-clinical translational PhD studentship – three years each

Neta Baruch
Siobhan Durran
Anna Gray
Amelie Pandraud

Clinical translational PhD studentships - three years each

Dr Adrian Miller
Dr Jasper Morrow

Centre administrator - five years

Zoë Scott

Clinical trial coordinator - five years

Gisela Barreto

Biobank technician - five years

Diana Johnson

MRI physicist - three years

Dr Chris Sinclair

Newcastle full time staff appointed following commencement of the Centre

Non clinical translational PhD studentships - four years each

Sally Spendiff
Alasdair Wood

Clinical trials coordinator - five years

Geoff Bell

Biobank technician - five years

Mojgan Reza

4. Clinical trials unit Centre for Neuromuscular Diseases

A major aim of the centre is to make clinical trials happen by providing a state of the art trials facility which includes a trial consultation room, neurophysiology equipment and a range of clinical trials, myometry, and exercise equipment including:

- Treadmill with un-weighting system
- Codamotion 3D movement analysis
- Cybex system
- Exercise ergometer
- Elliptical trainer
- Cortex metalyzer metabolic system – to measure aerobic capacity

The equipment in the trials unit has been specifically designed to harmonise with the Newcastle MRC Centre trials gym so that synchronous clinical trials in the North of England (Newcastle) and the South of England (Queen Square) can be undertaken throughout the MRC Centre, thereby enhancing collaboration and recruitment opportunities.

Many trials and interventions are planned or underway including:

- Collation of natural history information re physical disease progression
- Exercise intervention trials in muscle (mito) and nerve (CMT)
- Balance studies
- Gait and orthotic studies
- Fatigue studies
- Exercise physiology studies

Full details of active clinical trials mapping to the MRC Centre are listed in the next chapter.

5. Clinical trials supported by the Centre

Clinical trials linked to the MRC Centre and supported by different funding agencies including the Medical Research Council, Muscular Dystrophy Campaign, UK Department of Health, National Institutes of Health (USA), Food and Drug Administration (USA), AVI Biopharma and PTC Therapeutics.

Completed Trials

RESTORING DYSTROPHIN EXPRESSION IN DUCHENNE MUSCULAR DYSTROPHY: A PHASE I/II CLINICAL TRIAL USING AVI-4658

Status: Completed (closed to recruitment)

Sponsor: Imperial College London

Funder: Department of Health (DoH)

PIs: Prof. Muntoni Bushby

The primary scope of the trial is to assess efficacy (dystrophin production) and safety of intramuscular administered morpholino oligomer directed against exon 51 (AVI – 4658 PMO). Antisense therapy with the use of antisense oligomers has the potential to restore effectively the production of dystrophin, the defective protein, in >70% of DMD. This could result in increased life expectancy through improved muscle survival and function. Recent scientific research has demonstrated the potential of this technique to skip mutated dystrophin exons, restore the reading frame and generate functional dystrophin protein. Having demonstrated proof-of-principle in human cell culture and animal model studies, we now intend to determine efficacy and safety of this approach to induce dystrophin exon skipping in children with DMD. This study is aimed at children with Duchenne muscular dystrophy above the age of 10 years with mutations that can be rescued by the skipping of exon 51 [45-50; 47-50; 48-50; 49-50; 50; 52; 52-63].

RANDOMISED DOUBLE-BLIND PLACEBO CONTROLLED TRIAL OF LONG-TERM ASCORBIC ACID TREATMENT IN CHARCOT-MARIE-TOOTH DISEASE TYPE 1A

Status: Follow-up phase (closed to recruitment)

Sponsor: University College London

Funder: Muscular Dystrophy Campaign (MDC)

PI: Dr. Reilly

Charcot-Marie-Tooth disease 1A (CMT1A) is associated with a duplication of the peripheral myelin protein 22 (PMP22) gene. To date there is no pharmacological treatment for CMT1A patients. Treatments and therapy for CMT is restricted to symptomatic treatments such as physiotherapy and surgery for skeletal deformities. Recently, treatment with ascorbic acid (AA) has been shown to be effective for transgenic mice over-expressing PMP22, a model of the human disease. Treated animals had much less severe neuropathy as compared to untreated controls as shown by clinical and histological findings. Some clinical parameters even improved during treatment.

This is a phase III prospective, multi-centre, randomized, double-blind, placebo-controlled study aiming to evaluate the efficacy of AA treatment in CMT1A.

The study has been running now almost for two years and it is now in the follow-up phase. Fifty participants were enrolled in the UK site at the National Hospital for Neurology and Neurosurgery.

For information about the study please contact Dr. Matilde Laura at m.laura@ion.ucl.ac.uk.

Open Trials

THERAPEUTIC TRIAL OF MEXILETINE IN NON-DYSTROPHIC MYOTONIA

Full Title: A Phase II Randomized, Double-Blind, Placebo controlled, Cross-Over Study to Investigate the Efficacy of Mexiletine in Patients with Non-Dystrophic Myotonia

Status: Open to recruitment

Sponsor: University College London (UCL)

Start date: June 2009

Funder: Food and Drug Administration (FDA – USA)

PI: Prof. Hanna

The non-dystrophic myotonia (NDM) is a group of rare neuromuscular disorders that causes episodes of muscle stiffness (known as myotonias) and paralysis.

Predominantly the muscles of the face, hands and legs are affected. In addition to these episodes a permanent and debilitating muscle weakness can develop. The optimal treatment for these disorders is unknown.

Non-dystrophic myotonias are due to abnormalities of ion channels present in skeletal muscle membranes. There is experimental evidence that drugs like mexiletine which block the abnormal function of these ion channels allow the muscle to perform normally.

The study aims to test the efficacy of mexiletine in the treatment of the non-dystrophic myotonias. This proposal involves a multi-centre, double-blind, placebo-controlled cross over trial of a total duration of nine weeks. Approximately fifteen participants will be enrolled in the UK at the National Hospital for Neurology and Neurosurgery.

For information on the status of recruitment please contact Dr Dipa Raja Rayan at d.rajarayan@ion.ucl.ac.uk.

ECULIZUMAB FOR MYASTHENIA GRAVIS

Full Title: A Randomised, Double-Blind, Placebo-controlled, Cross-over, Multicenter Study of Eculizumab in Patients with Generalised Myasthenia Gravis (GMG) who have Moderate to Severe Muscle Weakness Despite Treatment with Immunosuppressants

Status: Open to recruitment

Sponsor: Alexion Pharmaceuticals, Inc.

Planned start date: Dec 09

Funder: National Institutes of Health (NIH - USA)

UK PI: Prof. Dimitri Kullmann

This is a randomized, double-blind, placebo-controlled, cross-over, multicenter study to evaluate the safety and efficacy of eculizumab for the treatment of patients with myasthenia gravis. There are four stages in the study, the Screening Period, the first Treatment Period, the Wash-Out Period, and the second Treatment Period (the cross-over Treatment Period). Myasthenia gravis (MG) is an acquired autoimmune syndrome caused by the failure of neuromuscular transmission, which results from the binding of autoantibodies to proteins involved in signalling at the neuromuscular junction (NMJ). These proteins include the nicotinic AChR or, less frequently, a

muscle-specific tyrosine kinase (MuSK) involved in AChR clustering. Current available treatments for myasthenia gravis aim to modulate neuromuscular transmission, to inhibit the production or effects of pathogenic antibodies, or to inhibit inflammatory cytokines. There is currently no specific treatment that corrects the autoimmune defect in MG.

Eculizumab is a humanized murine monoclonal antibody that blocks the activation of complement by selectively binding to C5 and preventing the enzymatic cleavage of C5 to C5a and C5b. The blockade of complement activation at this point in the cascade has been shown to prevent the proinflammatory effects of both C5a and C5b, especially the chemotaxis of inflammatory cells, and MAC (C5b-9)-mediated cell activation and lysis. Since eculizumab effectively inhibits complement, especially MAC formation, it is a potentially effective therapeutic approach for diseases such as MG in which the formation of the MAC and/or the release of C5a leads to localized destruction of the postsynaptic NMJ membrane and play a important role in the disease process.

Each patient who completes the study will receive approximately 22 infusions including 11 infusions of eculizumab and 11 infusions of placebo. The estimated duration of a patient's participation is approximately 41 weeks.

For more information about the study please contact Dr. Jennifer Spillane at j.spillane@ion.ucl.ac.uk.

DMD HEART PROTECTION TRIAL

Full-Title: A double-blind randomised multi-centre, placebo-controlled trial of combined ACE-inhibitor and beta-blocker therapy in preventing the development of cardiomyopathy in genetically characterised males with DMD *without* echo-detectable left ventricular dysfunction.

Status: Site Specific Approval pending

Sponsor: Newcastle NHS Foundation Trust

Planned start date: 2010

Funder: British Heart Foundation

PI: Dr John Bourke, Prof. Muntoni

Duchenne muscular dystrophy [DMD] is an X-linked recessively inherited neuromuscular disorder due to a deficiency in the expression of the protein dystrophin on the inner aspect of cell sarcolemma. Its clinical course has traditionally been characterized by progressive weakness of proximal limb-girdle muscles and calf muscle hypertrophy. Duchenne-affected individuals typically lose ambulation and become wheelchair dependent before the age of 13 and die from cardio-respiratory failure at around the age of 20 years. From the cardiology perspective, some 90% of males with DMD develop a severe, progressive form of cardiomyopathy. Twenty to 30% have evidence of left ventricular impairment on echocardiography by age 10 years.

Abnormalities in left ventricular function are evident in an even larger proportion of patients at all ages when more sensitive imaging techniques, such as tissue Doppler, magnetic resonance or metabolic imaging, are deployed. Despite the severity of cardiac involvement in DMD, cardiologists have largely ignored this particular inherited form of cardiomyopathy. This is due to the fact that, because of their inability to exercise, cardiac symptoms only occur terminally in DMD patients when all cardiac reserve has been eroded. Even today in most hospitals, cardio-active drug therapy is

only started in patients with DMD when overt heart failure is evident and, even then, is typically deployed tentatively for symptom control, without any expectation that it can prolong life.

The objective of this trial is to determine whether the introduction of ACE-inhibitor combined with beta-blocker therapy, before the onset of echo-detectable left ventricular dysfunction, can delay the age of onset and/or slow the rate of progression of cardiomyopathy compared to placebo in males with DMD. This is a double-blind randomized, placebo-controlled Phase III trial of combined ACE inhibitor and beta-blocker therapy (perindopril and bisoprolol) over a minimum of three years and a maximum of five years. 140 participants (70 per arm) are to be enrolled and randomised.

For more information about the study please contact trial coordinator Rahela Choudhury at r.choudhury@ich.ucl.ac.uk.

ARIMOCLOMOL FOR SPORADIC INCLUSION BODY MYOSITIS (IBM)

Full Title: A Randomized, Double-blinded, Placebo-controlled Pilot Study Assessing the Safety and Tolerability of Arimoclomol in Adult Patients with Sporadic Inclusion Body Myositis

Status: Open to recruitment

Sponsor: University College London (UCL)

Planned start date: June 2010

Funder: Medical Research Council (MRC)

PI: Prof. Hanna

Sporadic Inclusion Body Myositis (IBM) is the commonest acquired disease of muscle affecting people aged 50 years and over. This is a progressive and debilitating disease with both muscle weakness and wasting, characteristically of the quadriceps and finger flexors. Over time the condition can lead to severe disability, falls and swallowing impairment. Affected muscle tissue demonstrates inflammation and degeneration.

Arimoclomol is a new compound which acts by enhancing a normal, inbuilt protective cell reaction to stresses. The products of this response are 'Heat Shock Proteins (HSPs)' which counteract processes that end up leading to abnormal protein deposition and to damage mediated by inflammation.

This proposal involves a multi-centre, double-blind, placebo-controlled parallel study of total duration twelve weeks.

This study proposal aims to assess the safety and tolerability of Arimoclomol (100 mg TDS) as compared with placebo over 4 months of treatment in patients with IBM.

Recruitment will take place at the National Hospital for Neurology and Neurosurgery and twelve patients will be enrolled.

For information on the status of recruitment please contact Dr Adrian Miller at a.miller@ion.ucl.ac.uk.

A PHASE IIb EFFICACY AND SAFETY STUDY OF PTC124 IN SUBJECTS WITH NONSENSE MUTATION-MEDIATED DUCHENNE AND BECKER MUSCULAR DYSTROPHY

Status: Ongoing (closed to recruitment)

Sponsor: PTC Therapeutics

Funder: PTC Therapeutics

PIs: Prof. Bushby, Prof Muntoni

Duchenne muscular dystrophy (DMD) is an X-linked genetic disorder affecting young boys. The condition is disabling and life-threatening. A small subset of boys are classified as having Becker muscular dystrophy (BMD), a phenotypically milder form of the dystrophic muscle disease.

In approximately 10 to 15% of boys with DMD and BMD the causative defect is the presence of a nonsense mutation in the dystrophin gene that truncates dystrophin protein production by introducing a premature stop codon into the dystrophin messenger ribonucleic acid (mRNA).

PTC124 is a novel, orally bioavailable, small-molecule drug that promotes ribosomal read-through of mRNA containing a premature stop codon. Through this mechanism of action, PTC124 has the potential to overcome the genetic defect in boys for whom a nonsense mutation causes DMD/BMD.

In vitro studies in cell lines with dystrophin nonsense mutations have shown that PTC124 can restore production of the missing dystrophin gene.

This is an international, multi-centre, randomized, double-blind, placebo-controlled, dose-ranging, efficacy and safety study.

The study primary aim is to evaluate the effect of PTC124 on ambulation as assessed by the distance walked during a 6-minute walk test (6MWT).

The double-blind arm of the study randomised 174 participants worldwide which were followed for a period of 12 months. At the completion of the blinded treatment, eligible and compliant participants went on to receive PTC124 (Ataluren) in an open-label extension study. However, this study was prematurely discontinued based on a decision made by the Data Monitoring Committee, following the analysis of 6-minute walk-test (primary endpoint) data showing no statistical difference in placebo and active treatment in the main study. Dystrophin expression data is yet to be fully analysed.

(Ataluren is now the non-proprietary generic name for PTC124).

New PTC 124 in non-ambulant DMD has been suspended

PI Prof Katie Bushby

ANTISENSE OLIGONUCLEOTIDE INDUCED EXON SKIPPING IN DUCHENNE MUSCULAR DYSTROPHY

This initiative is led by the MDEX consortium (The MDEX consortium led by Professor Muntoni, is a multidisciplinary enterprise to promote translational research into muscular dystrophies, and is formed by the clinical groups of Professor Francesco Muntoni (UCL Institute of Child Health) and Professor Kate Bushby and Professor Volker Straub (Newcastle University), and scientists from Imperial College London (Professor Dominic Wells), UCL Institute of Child Health (Dr Jennifer Morgan), Royal Holloway University of London (Professor George Dickson and Dr Ian Graham),

HYP HOP: DICHLORPHENAMIDE vs. PLACEBO FOR PERIODIC PARALYSIS

Status: Open to recruitment

Sponsor: University College London (UCL)

Funder: National Institutes of Health (NIH - USA)

UK PI: Prof. Hanna

This is a phase III trial into Periodic Paralysis planned to start in 2010. This proposal involves a multi-centre, double-blind, placebo-controlled parallel group, nine-week studies comparing the effects of dichlorphenamide(DCP) vs placebo in patients with period paralysis (Hyper, Hypokalaemic periodic paralysis). The 9-week studies will investigate the prevention of attacks of weakness and it will be followed by 1-year double-blind extensions without placebo to compare the long term effects of DCP vs ACZ on the course of the diseases and on inter-attack weakness. Approximately 40 participants will be recruited from the United Kingdom.

For further information please contact Dr. James Burge at
James.burge@uclh.nhs.uk.

DOSE-RANGING STUDY OF AVI-4658 TO INDUCE DYSTROPHIN EXPRESSION IN SELECTED DUCHENNE MUSCULAR DYSTROPHY (DMD) PATIENTS – (Systemic study)Status: Ongoing (closed to recruitment).

Sponsor: AVI Biopharma

Funder: Medical Research Council (MRC) and AVI Biopharma

PIs: Prof. Muntoni Bushby

This is a safety study of AVI-4658 (a 30-base phosphorodiamidate Morpholino oligomer [PMO]), to skip exon 51 of the dystrophin gene in relevant subjects with DMD. This is an open-label, two-centre, dose-ranging comparative clinical study of duration twelve weeks.

The objectives of the study are to assess safety and to select the optimum dose that elicits at least 10% *de novo* dystrophin-positive fibres and dystrophin in a sentinel muscle group after an intravenous AVI-4658 dosing regimen. A total of up to 16 subjects (ambulatory paediatric males, aged ≥ 5 and ≤ 15 years of age) will be enrolled in this study, consisting of four treatment cohorts and four subjects per cohort. It is expected that there will be four treatment arms ranging from 0.5 mg/kg to 4 mg/kg. All subjects will receive 12 weekly intravenous infusions of AVI-4658. Precedent studies have demonstrate that AVI-4658 might have therapeutic relevance in managing DMD for boys whose frame-shifted dystrophin gene lesion could be restored after excision of exon 51 if sufficient drug is translocated into the nucleus of the afflicted muscle cell. This trial is being conducted in London and Newcastle. All participants have completed treatment. Analysis of results is ongoing. For further information please contact Guru Ganeshaguru, MDEX Clinical Trials Coordinator (Dr K. Ganeshaguru k.ganeshaguru@ich.ucl.ac.uk) or Geoff Bell, Trials Coordinator (MRC centre Newcastle site) at geoff.bell@nuth.nhs.uk.

CCRN 165 (NDS mito function)**Status: Open to recruitment****PI: Prof Chinnery**

A phase 2a, double blind, randomised, placebo-controlled, 28 day, two-arm, parallel group study of A0001 in patients with the A3243G mitochondrial DNA point mutation and evidence of impaired mitochondrial function.

PI – Professor P.F. Chinnery, Department of Neurology, Newcastle University, and Newcastle upon Tyne Foundation Hospitals NHS Trust.

The primary objective of this study is to establish proof of concept of the efficacy of A0001 in the treatment of patients with an established mitochondrial disorder using metabolic imaging, a number of functional assessments, biochemical measures and patient/clinical-rated scales.

DOSE-RANGING STUDY OF AVI-4658 TO INDUCE DYSTROPHIN EXPRESSION IN SELECTED DUCHENNE MUSCULAR DYSTROPHY (DMD) PATIENTS – (Systemic study) Status: Ongoing (closed to recruitment).**Sponsor: AVI Biopharma****Funder: Medical Research Council (MRC) and AVI Biopharma****PIs: Prof. Muntoni Bushby**

This is a safety study of AVI-4658 (a 30-base phosphorodiamidate Morpholino oligomer [PMO]), to skip exon 51 of the dystrophin gene in relevant subjects with DMD. This is an open-label, two-centre, dose-ranging comparative clinical study of duration twelve weeks.

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PI – Professor P.F. Chinnery, Department of Neurology, Newcastle University, and Newcastle upon Tyne Foundation Hospitals NHS Trust.

The primary objective of this study is to establish proof of concept of the efficacy of A0001 in the treatment of patients with an established mitochondrial disorder using metabolic imaging, a number of functional assessments, biochemical measures and patient/clinical-rated scales.

Secondary objectives of the study are to evaluate the tolerability and safety of A001 in this patient population and to establish pharmacokinetics of A0001 in this patient population.

Patients will be invited to participate if they fit the inclusion criteria which briefly consists of aged 18 – 70 (male or female), confirmed carriers of the A3243G mitochondrial DNA point mutation, with one or more of the associated symptoms and are capable of performing the required tests associated with this study (MRI, MRS, 6 minute walk test).

The study will recruit approximately 30 patients, which should ensure 21 (14 on treatment, 7 on placebo) evaluable patients, which will give sufficient power to detect an improvement of 50% on one of the outcome variables, the primary endpoint being improvement in the rate of ATP recovery in cardiac muscle as measured by P-MRS.

Following informed consent and screening, patients will be randomized to receive 28 days of either A0001 capsules (to be taken orally) at dose level of 0.75g BID (1.5g total daily dose) or placebo.

PK samples will be collected at Baseline and days 4,7,11,14,21 and 28

Safety will be evaluated by history updates, physical examinations, vital sign assessments, 12 lead ECG, routine blood lab analysis and adverse event assessments.

This study is open to recruitment, for further information contact P.F.Chinnery p.f.chinnery@newcastle.ac.uk, Dr G Gorman Grainne.Gorman@newcastle.ac.uk or Mr G Bell Geoffrey.bell@ncl.ac.uk

Exercise Studies

STRENGTHENING HIP MUSCLES TO IMPROVE WALKING DISTANCE IN PEOPLE WITH CHARCOT- MARIE-TOOTH DISEASE

Status: Closed to recruitment

Sponsor: University College London Hospitals

Funder: Muscular Dystrophy Campaign (MDC)

PI: Dr. Reilly

Charcot-Marie-Tooth (CMT) disease is a form of hereditary peripheral neuropathy. People with CMT present with weakness, wasting and sensory loss as a result of degeneration of the long peripheral nerves supplying the distal muscles.

The aim of this study will be to investigate the efficacy of a 16 week home based programme of training to increase hip flexor muscle strength and walking

endurance. Additional measures of gait speed, exertion, fatigue, disability and general activity will also be recorded. Baseline impairment measures will be obtained to ascertain predictors of strength gains.

This study will use a single blinded, randomized cross over design to investigate if training the hip flexor muscles will strengthen the hip flexor muscle and improve walking endurance in people with all types of CMT.

The trial will include people, aged between 18 and 70 years, who have been diagnosed with CMT on the basis of genetic tests (where possible), family history and neurophysiology testing. Each subject will be involved with the study for a 40 week period. For further information please contact Dr Gita Ramdharry, Research Physiotherapist at g.ramdharry@ion.ucl.ac.uk.

EXERCISE TRAINING IN PATIENTS WITH MITOCHONDRIAL DISEASE: ASSESSING THE BENEFITS

Status: Open to recruitment

Sponsor: University Newcastle

Funder: Muscular Dystrophy Campaign (MDC)

PI: Prof. Turnbull

Mitochondrial myopathies are a very important group of muscle diseases associated with weakness, pain and fatigue. At present, treatment options are very limited. Exercise therapy has been found to have some benefit in this group of patients and we wish to explore this further in terms of both strength and endurance.

The aim of this study is to demonstrate that strength exercise training is an effective approach to therapy in certain patients with mitochondrial myopathy, specifically those with sporadic mutations in mitochondrial DNA. Based on our previous research studies, we believe that such training will improve muscle strength, mitochondrial function, exercise tolerance and overall quality of life.

The main objectives will be:

- 1) To confirm that endurance training in patients with mitochondrial abnormalities improves quality of life, exercise tolerance and oxidative capacity.
- 2) To determine the ability of resistance muscle strength training to improve skeletal muscle strength and oxidative capacity by incorporation of satellite cells into mature myofibres.

Participants are expected to commit to an exercise training and testing over a period of 4 to 8 months.

The study will include patients between the ages of 18 and 65 years who have had a previous muscle biopsy showing a defect in skeletal muscle mitochondrial DNA that is either in the form of a sporadic point mutation or single large-scale deletion. Patients who have this type of mutation and do not have any family members that are affected and have no major cardiac involvement, hypertension, pulmonary or peripheral vascular disease that may complicate findings.

For information about recruitment contact Geoff Bell at geoff.bell@nuth.nhs.uk.

Open Natural History – Longitudinal Studies

NON-DYSTROPHIC MYOTONIAS: GENOTYPE AND PHENOTYPE CORRELATION AND LONGITUDINAL STUDIES

Status: Closed to recruitment

Sponsor: University College London

Funder: National Institutes of Health (NIH – USA)

UK PI: Prof. Hanna

This multi-centre project involves a prospective, cross-sectional and longitudinal natural history in non-dystrophic myotonias (NDM).

The aim is to collect standardized data from NDM patients, to include clinical symptoms, exam findings, as well as the results of strength, functional, and electrophysiological testing. Genetic testing will permit precise identification of individual NDM subtype. This information will allow for the identification and implementation of appropriate endpoints in studies of potential treatments. This is a NIH funded study. Twenty patients were enrolled at the National Hospital for Neurology and Neurosurgery.

For more information about the study please contact Dr Dipa Raja Rayan at d.rajarayan@ion.ucl.ac.uk.

ANDERSEN-TAWIL SYNDROME: GENOTYPE AND PHENOTYPE CORRELATION AND LONGITUDINAL STUDY

Status: Open to recruitment

Sponsor: University College London

Funder: National Institutes of Health (NIH – USA)

UK PI: Prof. Hanna

Andersen-Tawil syndrome is a neuromuscular disorder caused by a mutation in the KCNJ2 gene which codes for the inwardly rectifying potassium channel Kir2.1. A number of different mutations in this gene have already been identified in affected individuals. This disorder is characterized by the triad of periodic paralysis, developmental abnormalities and cardiac arrhythmias.

This project is a natural history trial into Andersen-Tawil Syndrome. The aim of the trial is to study the relationship between the genetic abnormalities underlying the disorder and the diverse clinical features.

Eight patients have been enrolled so far at the National Hospital for Neurology and Neurosurgery.

For more information about the study please contact Dr Dipa Raja Rayan at d.rajarayan@ion.ucl.ac.uk.

CHARCOT-MARIE-TOOTH DISEASE AND RELATED DISORDERS: A NATURAL HISTORY STUDY

Status: Open to recruitment

Sponsor: UCLH NHS Foundation Trust

Funder: National Institute of Health, USA

PI: Dr M Reilly

Co-PI: Prof F Muntoni, Dr M Laura

The main aims of this study are to:

Collect natural history data on CMT and related disorders Identify genetic

factors that cause and modify Charcot-Marie-Tooth neuropathies. CMT is the most common inherited neurological disorders for which there are no established treatments and there is a need to fully characterise the disease and the different genetic components.

Other aims are to:

Establish a scoring system for quantifying impairment in young children with various forms of CMT (most patients with CMT develop their first symptoms in the first two decades of life - in childhood).

The success of the paediatric scoring system will be determined by whether it can reproducibly quantify disease progression in children with various types of CMT.

Establish a Website Resource for the Inherited Neuropathies for patients, families and investigators.

For further information, please contact Rahela Choudhury at r.choudhury@ich.ucl.ac.uk.

Planned Trials

A PHASE II, DOUBLE BLIND, EXPLORATORY, PARALLEL-GROUP, PLACEBO CONTROLLED CLINICAL STUDY TO ASSESS TWO DOSING REGIMENS OF GSK2402968 FOR EFFICACY, SAFETY, TOLERABILITY AND PHARMACOKINETICS IN AMBULANT SUBJECTS WITH DUCHENNE MUSCULAR DYSTROPHY

Status: Set-up phase

Sponsor: GlaxoSmithKline

Funder: GlaxoSmithKline

PI: Profs F. Muntoni, V. Straub & K. Bushby

GSK2402968 has been explored at doses up to 6mg/kg subcutaneous (s.c.) weekly initially for 5 weeks in ambulant subjects with Duchenne Muscular Dystrophy (DMD). An open-label extension protocol is ongoing, and to date subjects have received GSK2402968 6mg/kg/week for at least 3 months.

GSK2402968 appears to be well-tolerated, and has the potential to be efficacious based on the dystrophin expression previously observed in muscle biopsies. However, more information is needed to determine dosing regimens for optimal therapeutic safety margin in relation to efficacy.

This study is designed to explore efficacy and safety of GSK2402968 given as a continuous regimen over 24 and 48 weeks. For further information please contact Rahela Choudhury, Clinical Trials Coordinator at r.choudhury@ich.ucl.ac.uk.

NOTE: GSK2402968 formerly known as PRO051

TAPP: THERAPEUTIC TRIAL OF POTASSIUM AND ACETAZOLAMIDE IN ANDERSEN-TAWIL SYNDROME

Status: Set-up Phase

Sponsor: University College London (UCL)

Funder: National Institutes of Health (NIH – USA)

UK PI: Prof Hanna

Andersen-Tawil Syndrome (ATS) is a rare form of periodic paralysis that is associated with serious heart-rhythm abnormalities. ATS is characterized by a triad of episodic muscle weakness, long-QT syndrome with potentially fatal cardiac dysrhythmias and skeletal developmental anomalies. The underlying cause of this potentially fatal condition is only partly understood and there are no established treatments. Mutations in the KCNJ2 gene encoding Kir2.1, an inward-rectifying potassium channel account for approximately 60% of ATS cases (termed ATS1), the remaining 40% are presumed to have an as yet undetermined gene lesion and are designated ATS2. ATS1 and ATS2 are phenotypically indistinguishable. The treatment of ATS has been largely anecdotal and empirical. This proposal involves a multi-centre, placebo-controlled 'n of 1' study design of total duration 45 weeks. The expected total enrolment for this multi-centre study is 16 participants. The aim of this study is to determine whether potassium supplements and/or acetazolamide alter the duration of muscle weakness and potentially life-threatening heart rhythm abnormalities in patients with ATS. For information on the status of recruitment please contact Dr. James Burge at James.burge@uclh.nhs.uk.

OUTCOME MEASURES IN SMA TYPE II AND III

Status: Set-up phase

Funder: SMA Europe

PI: Profs Muntoni, Straub, Bushby

This project provides an excellent opportunity as for the first time, ten leading neuromuscular centers in Europe which have been involved in the development and validation of functional scales for SMA will collaborate to validate and cross validate measures that have been suggested to be the most suitable for multicentric trials by a large international consensus, but have not been tested in large multicentric studies yet.

One hundred and thirty patients affected by type II and type III SMA will be enrolled and assessed at baseline and 6 and 12 months later. Non ambulant patients will be assessed using the modified version of the Hammersmith Motor Functional Scale while ambulant patients will be assessed using the extended module of the Hammersmith Motor Functional Scale and timed items, the 6 minute walk and a step activity monitor. All patients will also be assessed using the MFM, that covers the whole range of activities for both ambulant and non ambulant patients. All measures will undergo a process of validation including inter observer reliability. This information will be most valuable for any future trial and will make the groups involved ready to participate to future collaborative studies saving a lot of time on the preliminary aspects (validation, reliability, training) that will be fulfilled by the present study. The study will also provide natural history data for a 12 month period on patients. Please contact Rahela Choudhury, Clinical Trials Coordinator at r.choudhury@ich.ucl.ac.uk for further details.

PERIPHERAL NEUROPATHY OUTCOME MEASURES STANDARDISATION STUDY (PERINOMS)

Status: set-up phase

Sponsor: Erasmus Medical Center

PI: Dr M. Lunn

The current study aims to expand the clinimetric knowledge on outcome measures at various levels of outcome (pathology, impairment, activity & participation limitation, and quality of life) in autoimmune polyneuropathies, particularly in GBS, CIDP, MMN, MGUSP, and autoimmune small fibre neuropathies (AI-SFN). Also, the general applicability of an autonomic symptoms scale plus some selected activity limitation scales will be examined.

Outcome measures will be assessed in a cross-sectional and longitudinal group of patients at the level of:

- Pathology: Intraepidermal nerve fibre (IENF) density will be assessed in patients with GBS, CIDP, MGUSP, and AI-SFN (in sarcoidosis). IENF density will be examined regarding its correlation with other outcome measures (validity), its reliability (intra observer and inter-observer), and its responsiveness to clinical changes over time.

- Impairment: comparison studies, evaluating the validity, reliability, and responsiveness will be performed between MRC sumscore versus NIS motor subset, INCAT sensory sumscore versus NIS sensory sumscore, and hand-held Vigorimeter versus Jamar dynamometer. Also, the correlation of electrophysiological studies with other impairment outcome measures will be evaluated. Finally, the scientific soundness of the modified Dutch composite autonomic symptoms scale (mdCompass) will be examined.

- Activity limitation: comparison studies, evaluating the validity, reliability, and responsiveness will be performed between the ODSS and an overall neuropathy limitations scale (ONLS). Also, a newly devised weighted (based on Rasch analyses) activity and participation scale will be constructed, aiming specifically on the limitations in patients with polyneuropathy.

- Quality of life: Disease-specific versus generic quality of life measures will be assessed, determining their clinimetric soundness and by comparison studies in the various polyneuropathy groups.

The ultimate goal of the current study will be the presentation of a *specific* minimum core set of outcome measures to be used in future clinical and follow-up studies in patients with polyneuropathy, mainly those patients with autoimmune mediated polyneuropathies. The study will be performed in collaboration with several local, European, and USA neurological centres with great experience in dealing with inflammatory neurological disorders.

Imaging Studies

MRI in IBM and CMT

Full Title: A Study of Quantitative Magnetic Resonance Imaging and the Clinical Features of Inclusion Body Myositis and Charcot Marie Tooth

Disease Status: Open to recruitment

Sponsor: University College London Hospitals

Funder: Medical Research Council

PI: T Yousry / J Thornton / MM Reilly / M Koltzenburg / MG Hanna

Magnetic resonance imaging (MRI) is a key tool in the diagnosis and management of a number of diseases. Despite the wide use of MRI in several clinical settings, so far its role in neuromuscular disease has not been well established. The current standard for the diagnosis of neuromuscular disorders includes clinical examination, electrophysiological investigations, biopsy and genetic testing. Due to the nature of the involvement of prominent muscles and peripheral nerves in these disorders it is proposed that MRI could play a prominent role in understanding of neuromuscular disease.

This study aims to investigate the use of MRI as a tool in the study of nerve and muscle diseases by focusing on two particular neuromuscular diseases, one primarily neuropathic and one principally myopathic. Two separate patient cohorts with neuromuscular disease will be recruited. Forty patients with Sporadic Inclusion Body Myositis (IBM) will be recruited and 40 patients with genetically confirmed Charcot Marie Tooth Disease (CMT) will be recruited. In addition to the two patient cohorts, two groups of healthy volunteers each of size 40 will act as comparators for the disease groups. Each of the patients enrolled in the study will undergo an MRI scanning session in which the quantitative MR techniques developed in Phase 1 with the health volunteers will be applied. In addition to the MRI scanning sessions, each patient will undergo a clinical examination to record the main clinical features of their disease status including an electrophysiological nerve conduction assessment. In the final phase of the study, a sub-group of the patients will then be followed-up at 6 month intervals for 5 years in a longitudinal natural history study of IBM and CMT that focuses on the MR methods and clinical findings that were shown to be most illuminating.

Changes over time in the MRI parameters in the diseased groups and Healthy volunteers will be compared.

Objectives:

To detect, using quantitative magnetic resonance imaging (qMRI), the changes in the nerves and muscles of patients with inclusion body myositis or Charcot Marie Tooth disease, and to relate these changes to the measurable clinical and neurophysiological features in these diseases. This will allow the value of qMRI techniques as markers of disease activity and progression to be tested.

Secondary objectives of the study include:

- The development of novel quantitative MR techniques for targeted assessment of the human neuromuscular system
- To more fully characterize both the magnetic resonance imaging and clinical features of inclusion body myositis or Charcot Marie Tooth disease as compared with healthy individuals and to study the progression of these characteristics with time over a period of 5 years.

For more information about the study please contact Dr. Jasper Morrow at j.morrow@ion.ucl.ac.uk.

Full-Title: A study using Magnetic Resonance Imaging (MRI) and Magnetic Resonance Spectroscopy (MRS) in Patients with Limb Girdle Muscular Dystrophy 2I; an assessment of muscle damage.

Status: Open to recruitment

Sponsor: Newcastle upon Tyne NHS Trust

Funder: MRC Centre for Neuromuscular diseases

PI: Prof. Volker Straub

Re-defined in 1995, the LGMDs are face sparing, proximally predominant, progressive muscular dystrophies with elevated creatine kinase levels and dystrophic features on muscle biopsy. In the current classification system, LGMDs are divided into autosomal dominant (LGMD1) and autosomal recessive (LGMD2) disorders with a superimposed lettering system denoting the chronological order of the chromosomal linkage.

Limb Girdle Muscular Dystrophy 2I (LGMD2I) is caused by a mutation in the fukutin related protein gene (FKRP)¹ and manifests temporal variability. Clinically the age of onset, rate of progression and severity varies greatly between cases and even within the same family. They range from asymptomatic patients with mildly raised creatine kinase levels to those severely affected and non ambulant. The respiratory and cardiac complications, well known to occur in this type of muscular dystrophy, in 30% and 60% of patients respectively, occur independently of the general muscle weakness and also cardiac complications occur independently from respiratory compromise.

Magnetic Resonance imaging (MRI) has been increasingly used in imaging in patients with neuromuscular disorders over the past 5 years.

Studies have shown that whilst there is considerable overlap in muscle involvement there is also striking differences that can be of diagnostic value. In both patients with LGMD2A and LGMD2I there is a prominent pattern of involvement of the posterior thigh muscles, however in LGMD2A there is also selective involvement of the medial gastrocnemius and soleus muscles in the lower leg, which was not seen in LGMD2I. Although it is clearly demonstrated that MRI findings mirror those obtained from clinical examination, it has been reported recently that in fact MRI abnormalities can be detected in patients with neuromuscular disorders when clinical examination of particular muscle groups have been normal. MRI can therefore be useful to show early manifestations of a disease and to monitor the effect of early therapeutic interventions.

Beside MRI another non-invasive technique to consider is phosphorus magnetic resonance spectroscopy (P-MRS). P-MRS studies have demonstrated several metabolic abnormalities in the skeletal muscle of patients with Duchenne Muscular Dystrophy (DMD)/ Becker Muscular Dystrophy (BMD) and in the group of autosomal recessive LGMDs, associated with sarcoglycan deficiency (LGMD2C-F). These changes are thought to be specific for dystrophies secondary to deficits in the dystrophin-glycoprotein complex. In these patients there appears to be an increased cytosolic pH in both groups, however there is also abnormal concentrations of phosphorylated compounds (in particular, decreased phosphocreatine and increased inorganic phosphate concentrations).

The study overall aim is to develop and evaluate non-invasive techniques to quantify muscle pathology and the rate of change over time in LGMD2I, which is potentially a useful tool for monitoring response to treatment and therapies. This shall be achieved by measuring static MRI over a 2 year period and comparing this to age matched adult controls including the quantitative 3-point Dixon technique for measuring fat. At the same time we will also be measuring the Pi and cytosolic pH, ATP and ADP via MRS to see whether a specific pattern of metabolic abnormality is detected in these patients.

For further information about the study please contact Dr. Jasper Morrow at j.morrow@ion.ucl.ac.uk.

6. The Cochrane Neuromuscular Disease Group

The Cochrane Neuromuscular Disease Group (CNDG) is part of the Cochrane collaboration which produces and disseminates systematic reviews of healthcare interventions, and promotes the search for evidence in the form of clinical trials and other studies of interventions.

Registered with the Cochrane Collaboration in 1998 with its editorial base in King's College London, the Group moved to the MRC Centre in September 2008.

Aims

The Group aims to provide systematic reviews of all interventions for all neuromuscular diseases, including amyotrophic lateral sclerosis/motor neuron disease, peripheral nerve disorders, myasthenia gravis and neuromuscular function disorders, and muscle diseases.

Activity

In 10 years the CNDG has published 73 systematic reviews and 40 protocols (pre-reviews). The conditions most prevalent, lethal or seriously disabling have each been topics for multiple reviews with different sets of interventions. Developments include projects on reviews of Diagnostic Test Accuracy and now Overviews of Reviews which will pull together the multiple interventions for one condition under a single umbrella to increase accessibility to the information for healthcare professionals, policy makers and patients.

Further information about the work of the Group can be found on its website <http://www.neuromuscular.cochrane.org>

CNDG Staff

Professor Richard Hughes

Dr Michael Lunn

Kate Jewitt

Angela Gunn

Rachel Barton

Co-ordinating Editor

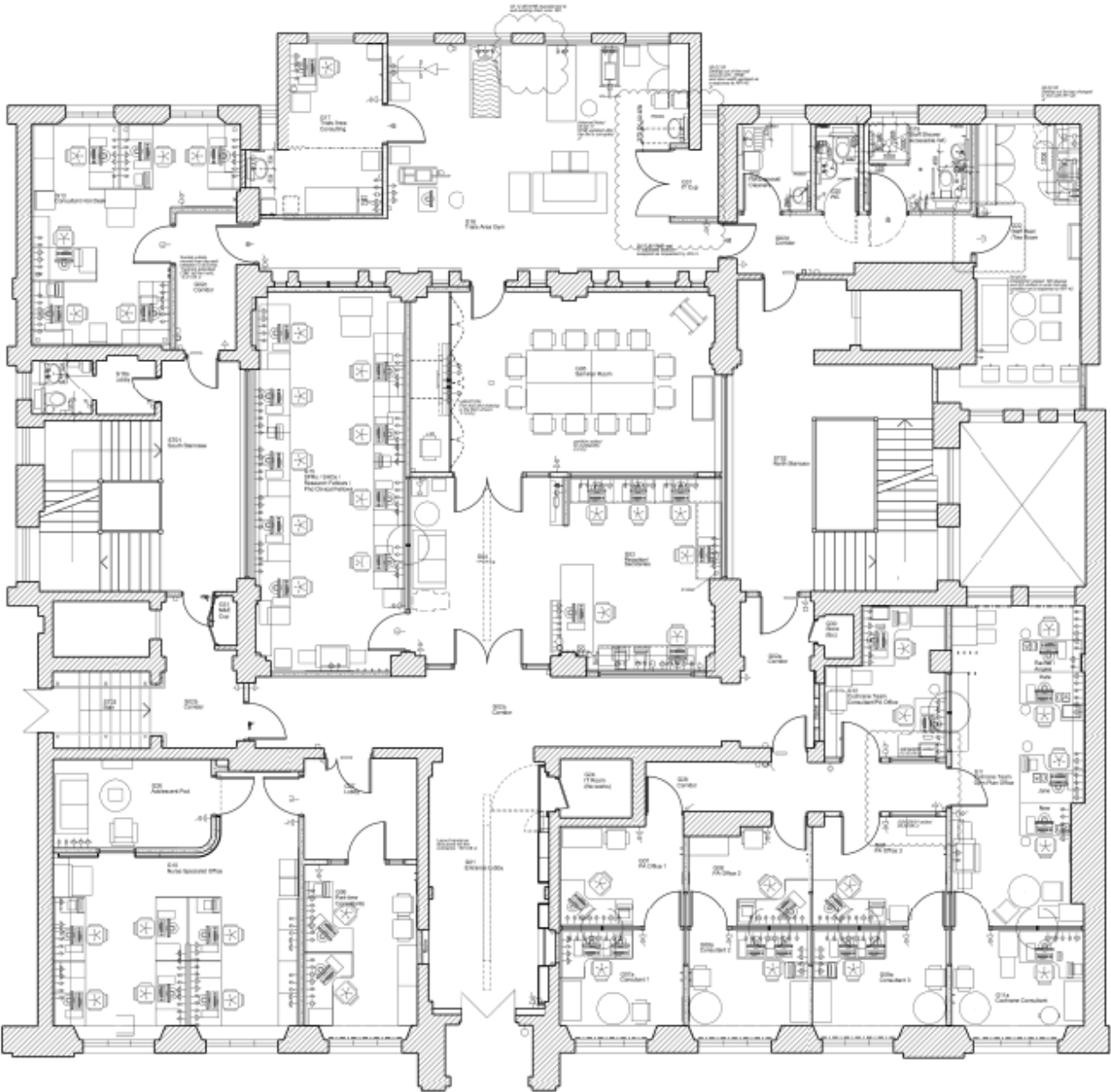
Co-ordinating Editor

Managing Editor

Trials Search Coordinator

Assistant Trials Search Coordinator

7. Floor plan and photo gallery









Who's who in the Centre for Neuromuscular Diseases



Gisela Barreto

Gisela Barreto has worked as a Trials Coordinator in the MRC Centre for Neuromuscular Diseases since February 2008. Her portfolio includes both commercial and non-commercial trials. She has a MEng in Medical Engineering from Queen Mary & Westfield College, University of London. Previously she has worked in cancer trials at the Institute of Cancer Research and also in phase I trials at Quintiles (CRO).

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Rachel Barton

Rachel Barton is one of two Trial Search Co-ordinators who support reviewers in designing and running search strategies on bibliographic databases such as MEDLINE. She moved with the Cochrane Group to Queen Square in 2008, and has previously worked as an NHS librarian.

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Michelle Bovell

Michelle Bovell is Medical Secretary to Dr Mary M Reilly. MRC Centre for Neuromuscular Diseases, and Medical Secretary to Karen Bull – Clinical Nurse Specialist. She works closely with Carol Brown, PA to Dr Reilly.

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Carol Brown

Carol Brown joined the Peripheral Nerve Team in September 2004 as PA to Professor Mary Reilly. She has seen the team evolve into the MRC Centre for Neuromuscular Diseases (the joining of the Peripheral Nerve Team and the Muscle Team) and supports Dr Reilly in her clinical work, and also some of her research work. She enjoys the diversity of the Centre's work and also the interaction between clinical and academic staff.

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Karen Bull

Karen Bull Joined the team as a Clinical Nurse Specialist for neuromuscular disorders four years ago. In this time she has developed a specialist interest in the care of the peripheral nerve patients, offering support education and monitoring of the client group. Prior to joining the team she has had a varied career which has included general medical and paediatric experience. She developed an interest in neurology, and prior to joining the team spent 14 years in general neurology, the last six of which were spent as the ward manager for neuro-medical patients and stroke rehabilitation.

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James Burge

Dr James Burge is a Specialist Registrar in Clinical Neurophysiology at the National Hospital for Neurology and Neurosurgery, and started a PhD under the supervision of Prof. Hanna in September 2008. He is studying mutations in the chloride channel, *CLIC1*, that cause Myotonia Congenita, and developing a skeletal muscle expression system that will facilitate pre-clinical testing of novel therapies for the disease.

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Jan Clarke

Jan Clarke is the motor neurone disease clinical nurse specialist and works closely with Robin Howard, Katie Sidle and Richard Orrell.

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Liz Dewar

Liz is a senior physiotherapist working in the MRC Centre for NMD. She has worked in the NHNN since 2001 and specifically within the Neuromuscular team since 2007. She is involved in providing specialist physiotherapy assessment and advice for people with Neuromuscular conditions and also assists in some of the clinical research trials run by the Centre.

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Helen Eddlestone

Helen Eddelstone is the respiratory clinical nurse specialist and works closely with Dr Hirsch.

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Marcia Forde

Marcia Forde is Secretary to Dr Matt Parton, Consultant Neurologist in the muscle team at the Centre for Neuromuscular Diseases.

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Dr Lionel Ginsberg

Dr Lionel Ginsberg is a consultant neurologist at the Royal Free Hospital and National Hospital for Neurology and Neurosurgery. He has a special interest in neuropathy and metabolic neuromuscular diseases.

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Anne Grayson

Anne Grayson has been PA to Professor Hanna for the last ten years.

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Stephanie Grisdale

Stephanie Grisdale is PA to Dr Lunn and Dr Manji in the Centre.

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Angela Gunn

Angela Gunn is one of two Trial Search Co-ordinators who support reviewers in designing and running search strategies on bibliographic databases such as MEDLINE. She moved with the Cochrane Group to Queen Square in 2008, and has previously worked as an NHS librarian.

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Mike Hanna

Professor Hanna is a Consultant Neurologist and Director of the MRC Centre. He runs the specialist muscle services and the Nationally Commissioned services for mitochondrial diseases and Muscle channelopathies in partnership with the muscle clinical team Dr Chris Turner, Dr Matt Parton, Dr Shamima Rahman, Dr Janice Holton, Liz Dewar, Cath Parry and Georgie Mewing. He undertakes clinical and genetic research in muscle diseases. He is the Queen Square Divisional Clinical Director.

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Nick Hirsch

Dr Nick Hirsch is Consultant Anaesthetist and Head of the medical neurological ITU. He specialises in respiratory failure in neuromuscular and neurological diseases and runs the myasthenia service in partnership with Dr Robin Howard and Professor Dimitri Kullmann. He leads the Queen Square home ventilation support service.

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Robin Howard

Dr Robin Howard is a consultant neurologist and runs the specialist motor neurone disease service in partnership with Dr Katie Sidle. He is a specialist in neurological intensive care and has published widely on many aspects of neuromuscular diseases.

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Richard Hughes

Professor Richard Hughes has been Visiting Professor of Neurology in the MRC Neuromuscular Disease Centre since November 2007. With Michael Lunn, he is joint co-ordinating editor of the Cochrane Neuromuscular Disease Review Group until April 2010 after which he will remain an editor. His main research interests are treatment for inflammatory neuropathy and systematic reviews of neuromuscular disease.

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Elsbeth Hutton

Dr Elspeth Hutton is an Australian Neurologist, who moved to Queen Square in 2007 to take up a post as the Australian and New Zealand Neurology Fellow. A Clinical Research Fellow with an interest in neuropathic pain, she is currently studying potential cutaneous neuroimmune mechanisms in neuropathic pain with Dr Michael Lunn and Prof Martin Koltzenburg.

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Martin Koltzenburg

Professor Martin Koltzenburg is Head of Clinical neurophysiology and undertakes research into small fibre neuropathy, pain and neuromuscular channelopathies. He is Deputy Director of the MRC Centre for Neuromuscular Diseases.

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Dimitri Kullmann

Professor Dimitri Kullmann's main research interests are neurological channelopathies, myasthenia gravis, neurocritical care and basic science of neuronal signalling. He runs the clinical myasthenia gravis service in partnership with Dr Nick Hirsch and Dr Robin Howard.

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Matilde Laurá

Dr Matilde Laurá has worked as a Clinical Research Fellow since 2006. Her interests are peripheral neuropathies and in particular inherited neuropathies. Together with Dr Mary Reilly she carried out the Ascorbic Acid trial for patients with Charcot-Marie-Tooth disease type 1A.

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Michael Lunn

Dr Michael Lunn was appointed as consultant neurologist in 2005. He has an interest in inflammatory neuropathies and his research has concerned Guillain-Barre syndrome, CIDP and paraproteinaemic neuropathies. He is also clinical lead in neuroimmunology and Coordinating Editor of the Cochrane Neuromuscular Disease Group, now based in the MRC Centre.

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Pedro Machado

Dr Pedro Machado is a Clinical Research Fellow and Rheumatology Specialty Trainee. He has a research background that includes clinical epidemiology, systematic reviews and outcome research. With Professor Michael Hanna, he is involved in clinical studies of Inclusion Body Myositis (IBM), namely the Arimoclomol trial for patients with IBM and the MRC Centre IBM Research Clinic.



Hadi Manji

Dr Hadi Manji is a Consultant Neurologist and Senior Lecturer. He qualified in 1982, Trinity Hall Cambridge and Middlesex Hospital, and trained in Neurology at National Hospital, Queen Square and L'Hopital Kremlin Bicetre, Paris. He was appointed Consultant in 1997. His main interests are in infectious and inflammatory peripheral nerve disorders. Other interests include neurological infections including HIV. He was Chief author and editor of the Oxford Handbook of Neurology published in 2007.

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**Sarah Mazdon**

Sarah Mazdon is PA to Dr Robin Howard.

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**Georgie Mewing**

Georgie Mewing joined the Centre two years ago in the new post of Clinical Support Nurse. She is originally from Australia and has experience in many different specialities of nursing, however has taken a special interest in neuromuscular diseases.

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**Adrian Miller**

Dr Adrian Miller is a Clinical Research Fellow and Neurology Specialty Trainee. With Professor Linda Greensmith, he uses *in vitro* disease models to research potential therapeutic mechanisms for Inclusion Body Myositis (IBM). He is also involved in several national and international clinical studies of IBM, with Professor Mike Hanna, and in the MRC Centre IBM Research Clinic.

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**Jasper Morrow**

Dr Jasper Morrow is a Clinical Research Fellow in Neuromuscular MRI. His research involves investigating new MRI techniques to better describe and quantify inherited and acquired neuromuscular diseases. He came to Queen Square from New Zealand in August 2008, and has been working at the centre for neuromuscular diseases since August 2009.

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**Sinead Murphy**

Dr Sinead Murphy joined the Centre in July 2009 as a Clinical Research Fellow. In July 2010 she was awarded with an NIH-funded fellowship in inherited neuropathies from the Rare Disease Inherited Neuropathy Consortium. This one-year fellowship will allow her gain further expertise in genetic neuropathies as well as undertake a specific research project investigating X-inactivation in X-linked Charcot-Marie-Tooth disease (CMT). She is also involved in research into the genetic causes of CMT, distal hereditary motor neuropathy and hereditary sensory neuropathy.

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Richard Orrell

Dr Richard Orrell has longstanding clinical and research interests in the wide range of neuromuscular disorders. This includes genetic, inflammatory, and degenerative conditions of muscle and nerve. He is particularly interested in motor neuron diseases, including amyotrophic lateral sclerosis. He is a consultant neurologist and runs the motor neurone disease service in partnership with Robin Howard and Katie Sidle.

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Catherine Parry

Catherine Parry joined the team as a Clinical Nurse Specialist for neuromuscular disorders five years ago. In this time she has developed a specialist interest in the care of patients with muscle disease, in particular the areas of mitochondrial muscle disease, muscle channel disease and transition of care. Prior to joining the team she has had a varied career working in acute medicine and critical care settings. She developed an interest in neuromuscular disease when she spent 8 years previous to joining the team working on a long term ventilation unit, of which the last 18 months were spent as the Ward Manager. As well, she helped set up and develop a clinic specifically for patients with Duchenne Muscular Dystrophy and their families and worked on a Trust project for improving transition of care.

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Matt Parton

Dr Matt Parton has been a consultant neurologist since 2006. Together with Professor Mike Hanna and Dr Chris Turner, he provides regular specialist muscle disease clinics. His particular interests in the service are in inclusion body myositis, the management of immune-mediated myositis and investigation of hereditary dystrophies. He is the clinical governance lead for the neuromuscular service. He also works as a general neurologist at Whipps Cross Hospital in East London and has wider interests in teaching and training.

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Dr Rob Pitceathly

Rob Pitceathly is a Clinical Research Fellow in Mitochondrial disease working for Professor Michael Hanna and Dr Shamima Rahman at the MRC Centre for Neuromuscular Diseases. He is currently recruiting patients with mitochondrial disease to a national database as part of a collaborative cohort study with colleagues at the MRC Centre for Neuromuscular Diseases in Newcastle.

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**Vina Pswarayi**

Vina Pswarayi is the NCG mitochondrial and channel co-ordinator who answers and addresses all queries of an NCG nature

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**Shamima Rahman**

Dr Shamima Rahman is DH/HEFCE Senior Lecturer at the UCL Institute of Child Health, Honorary Consultant in Mitochondrial Medicine at NHNN and Honorary Consultant in Paediatric Metabolic Medicine at Great Ormond Street Hospital (GOS). With Professor Mike Hanna, she runs the London National Commissioning Group (NCG)-funded clinical service for Rare Mitochondrial Diseases in Adults and Children (fortnightly adult mitochondrial clinic at NHNN and fortnightly paediatric mitochondrial clinic at GOS). Her research interests include molecular mechanisms underlying primary mitochondrial diseases (both mitochondrial DNA and nuclear gene-encoded); natural history of mitochondrial diseases; mitochondrial deafness and genetic susceptibility to aminoglycoside-mediated ototoxicity; and small molecule therapy of mitochondrial diseases.

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**Dipa Raja Rayan**

Dr Dipa Raja Rayan is a a neurology trainee clinical research fellow undertaking a PhD in muscle channelopathies with Professor Hanna.

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**Gita Ramdharry**

Dr Gita Ramdharry has worked as a physiotherapist since 1995 and developed a special interest in neurology early on. She worked as a clinical physiotherapist at the NHNN on 2001 and moved into research at the ION in 2004. She completed a PhD in 2008 looking at walking patterns, endurance and orthotic interventions for people with Charcot-Marie-Tooth disease. She is now a part-time honorary researcher at the MRC centre; the rest of her time is spent as a lecturer at the School of Physiotherapy at St George's University of London.

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Mary Reilly

Professor Mary Reilly is a consultant neurologist and lead for the peripheral nerve service. She is interested clinically in all forms of neuropathies but has a particular interest in inherited neuropathies such as Charcot-Marie Tooth Disease. She is currently conducting genetic lab and clinical based research and clinical trials in this area.

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Alex Rossor

Dr Alex Rossor is a clinical research fellow. With Professor Mary Reilly and Dr Henry Houlden he is helping to characterise the phenotype of patients with distal hereditary motor neuropathy (dHMN). He is also working with Professor Greensmith to create a primary motor neuron model of dHMN due to mutations in the HSPB1 gene.

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Penny Schafer

Penny Schafer is secretary to Dr Chris Turner for the muscle service in the centre.

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Anthony Schapira

Professor Schapira's research area in neuromuscular disease is within the mitochondrial myopathies, particularly in the area of mitochondrial DNA depletion syndromes and mitochondrial involvement in neurodegenerative disorders. He has been at Queen Square since 1984 and has been a Professor at Queen Square since 1990.

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Zoë Scott

Zoë has been Centre Senior Administrator of the MRC Centre for Neuromuscular Diseases since March 2008, and works with Professor Hanna, Professor Reilly and other members of the Steering Committee in London and Newcastle, coordinating all aspects of the Centre's activities.

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**Katie Sidle**

Dr Sidle is a consultant neurologist specializing in the field of Motor Neurone Disease (MND). The NHNN is the MND Association regional care centre for patients with MND and she is responsible for the care of patients with MND in the weekly MND clinic. She has a background in molecular genetics and is currently developing research interests in the field of MND with colleagues within the neighbouring Institute of Neurology.

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**Chris Sinclair**

Dr Chris Sinclair, the centre MRI Physicist, came to Queen Square in 2008 to work on neuromuscular magnetic resonance imaging (MRI). He is principally involved in developing advanced quantitative MRI techniques for application in neuromuscular diseases, including several patient studies within the centre.

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**Jennifer Spillane**

Dr Jennifer Spillane is the John Newsom Davis clinical research fellow in myasthenia gravis undertaking a PhD in the centre.

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**Chris Turner**

Dr Chris Turner has been working as a consultant at the MRC Neuromuscular Centre and UCLH since 2007. He has a specialist interest in muscle disease and runs a twice monthly myotonic dystrophy clinic at Queen Square

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9. Running the Centre

Consultant Leadership Team

A monthly consultant leadership team will meet to consider all aspects related to running the Centre. There will be an agenda which will include, but not be limited to , the following standing items:

- Allocation of space in the centre.
- Consideration of applications for trials using centre facilities
- Maintenance of the centre website
- Production of the annual centre brochure
- Links with the Cochrane unit
- Links with the MRC Centre
- Fundraising
- Staffing
- Maintenance of infrastructure including the trials equipment
- Centre database and coordinator
- Blue sky for the centre-phase II etc

The consultant leadership team will be in addition to the regular team and leadership meetings which include:

- MRC Centre steering committee
- NCG mitochondrial and Muscle channel MDT meetings
- Muscle team MDT
- Peripheral Nerve team MDT
- Peripheral Nerve genetic meeting
- Muscle pathology meeting
- Peripheral Nerve pathology meeting
- Neuroimmunology team meeting

Booking rooms in the centre

It is essential that all usage of seminar rooms and trials consultation room facilities are booked in advance.

Seminar room:	Anne Grayson	x713014
Trials room:	Carol Brown	x713457

For help using the audiovisual facilities in the seminar room please contact Anne Grayson or Zoë Scott.

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