Muscular Dystrophy UK's research magazine
2019

Target Research

Genome editing

Could it be a treatment for muscle-wasting conditions?

Patient preferences

Find out how we're helping to integrate the patient voice in drug development

MDUK research programme

Read about the pioneering research MDUK is funding across a range of conditions

Muscular Dystrophy UK
Fighting muscle-wasting conditions

About us

Over 70,000 children and adults live with a muscle-wasting condition in the UK today. There's no cure, it limits and, in many cases, shortens lives.

Muscular Dystrophy UK funds pioneering research into treatments and cures to improve lives today and transform those for future generations. We're here with information, advice and support to help people with or affected by the condition to live well with muscular dystrophy. And we're driving change to see better care so that people can stay active, independent and connected.

With your support, we can be here for everyone affected today, tomorrow and beyond. Together we will beat muscular dystrophy.

Contents

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Welcome

As usual, you'll find an annual snapshot of how your support powers our research, and how these projects contribute to the development of potential treatments. In 2018, we invested £1.2 million in 10 new projects that came through our grant round. This wouldn't have been possible without the generosity of our supporters, so many thanks for helping us to fund this essential research.

You'll read about genome editing, and how it is being used in research into muscle-wasting conditions. We've received a lot of questions about this topic recently, so thought it would be useful to cover it in more detail and to try to separate the facts from the fiction.

You'll also read about how MDUK is working with pharmaceutical companies, academics, patients, healthy technology assessment bodies and regulatory authorities to find ways to give patients a voice in drug development. This is part of an international five-year project called PREFER.

As always, please do get in touch if you have any questions or feedback on this edition, or ideas for the next.

Jenny

Dr Jenny Sharpe
Editor, 020 7803 2885
research@musculardystrophyuk.org

A word from our Director

For those of you I haven't met, I'd like to take this opportunity to introduce myself. I joined MDUK in June 2018 as the Director of Research and Innovation. Previously I was the Head of Neurosciences and Mental Health at the Medical Research Council and I have over 10 years of experience in research funding.

Over my first six months, I've been busy attending conferences and building relationships with scientists, clinicians, funding organisations, pharmaceutical companies and policy-makers. The World Muscle Society meeting was a particularly good way to hear the latest progress in neuromuscular research and to meet some of the leading researchers.

I've also spoken to families and individuals from around the country at various MDUK events, including the National and Scottish conferences, Cambridge Town and Gown and other regional events. I hope to meet more of you in the coming months.

I'm excited to tell you that soon we'll be launching our new research strategy, which complements MDUK's strategy *Making every day count* and outlines our research priorities for the next three years. These focus on harnessing the power of genetics, increasing our understanding of the disease mechanism, facilitating drug development and improving quality of life. We will underpin all of this work with our commitment to partnerships and innovation, and to supporting excellent researchers, particularly those in the earlier stages of their careers.

The full document will be posted on our website in the coming months, and look out for a future edition of *Target MD*, where we'll be sharing a summarised version of it.

Wishing you all the best for 2019!

DK Adcock

Dr Kate Adcock
Director of Research and Innovation, Muscular Dystrophy UK

Genome editing

Genome editing is considered to have great potential for treating numerous health conditions, including muscle-wasting conditions. Read on to understand more about genome editing, and where the progress is being made.

What is genome editing?

Genome editing allows scientists to change the DNA, in other words the molecule that contains the genetic code, of cells or whole organisms. It can be used to add, remove or replace DNA. If changes are made within a gene, the technique is sometimes referred to as gene editing.

There are several genome editing techniques that scientists can use. Although they differ in cost, efficiency and accuracy, they all share a common component – an enzyme called a 'nuclease'. This enzyme cuts the DNA at a specific location, acting like a pair of molecular scissors. The cell then re-joins the DNA through its own natural repair processes.

The most commonly-used genome editing system is CRISPR/Cas9, which was originally discovered in bacteria as a natural defence against viruses. You can think of it as 'a guided missile, targeting precise sites' in the genome. The Cas9 nuclease acts like the missile, while the CRISPR part is the guidance system, telling Cas9 where to hit.

What is genome editing used for?

Currently, it's mostly used in research. But given that it has the potential to alter any DNA sequence – in bacteria, plants, animals or humans – it could also be used in:

- medicine, to treat or prevent a genetic disease
- agriculture, to protect crops from drought or disease
- environment, to control insect populations that transmit diseases
- industry, for biofuel or chemical production.

In research, scientists also use genome editing to understand what genes do and how they contribute to the way we are. For example, scientists may try to model a human disease in cells or animals by deleting or editing a gene thought to contribute to the disease. If these models do mimic the disease, they could then be used to test new therapies.

What's the difference between gene therapy and genome editing?

Broadly speaking, gene therapy is the use of genetic material to treat a disease. Depending on the disease, this could involve:

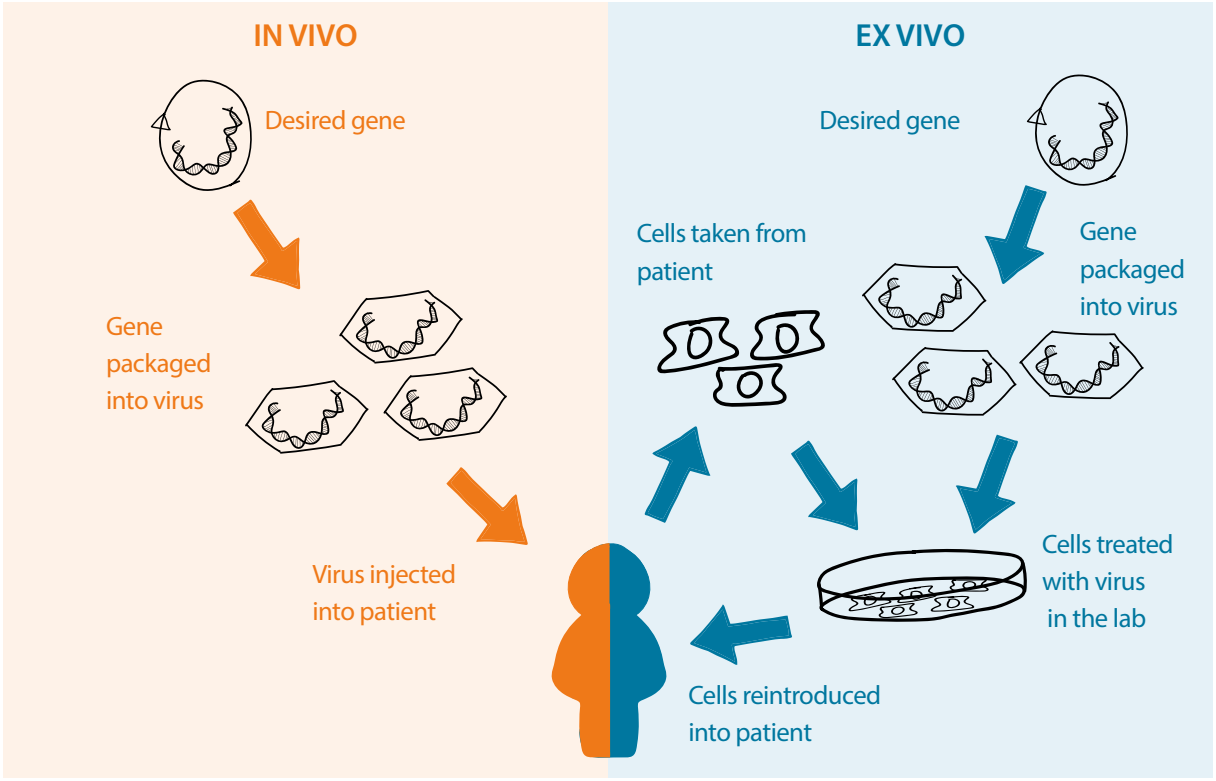
- introducing new genes, in order to boost production of a desired protein
- correcting mutated genes, so that they are functional again
- silencing genes that are causing problems.

Genome editing is a form of gene therapy when it's used to treat a disease. This sort of therapy can be injected directly into a patient (in vivo), or into cells from a patient (ex vivo), which are then transplanted back into the patient (see figure). Researchers around the world are investigating the potential of genome editing as a treatment for muscle-wasting conditions. We'll touch on this later in the article.

What are the challenges with genome editing?

Although the molecular scissors are targeted to a specific point in the genome, they can sometimes cut in the wrong place – this is known as an off-target effect. Off-target effects could be dangerous if they disrupt healthy genes or important regulatory DNA.

Types of gene therapy



Although there has been a lot of research to refine genome editing techniques, we still don't fully understand the risk of off-target effects. Scientists need to address this before we can use genome editing in the clinic.

Another challenge is how to get the genome editing system into the cells of the body. It can't travel around in the blood like other drugs can, as its constituent parts are too large. It needs to be packaged up into something called a 'vector', which can enter cells more easily. Several vectors are being investigated, including different types of viruses and tiny molecules called nanoparticles.

Why is genome editing controversial?

In addition to questions about its safety, there are some ethical concerns about genome editing. If genome editing were used to change the DNA of a human embryo, these changes would be hereditary, in other words they would be passed down to that person's children and to future generations. Some people have moral and religious objections to manipulating embryos in this way. Currently, researchers in the UK need to have a licence from the Human Fertilisation and Embryology Authority to carry out genome editing in human embryos. However, it is illegal to keep the embryos beyond 14 days after fertilisation, and they cannot be transferred into a person.

A recent survey by the Royal Society showed that the majority of the UK public supported the use of genome editing to treat incurable diseases. However, there is a concern that this could lead us down a 'slippery slope' to using it for cosmetic reasons or enhancing abilities. It's important that scientists, clinicians, regulators, policy-makers, patients and the general public continue to discuss these issues and shape the UK's policy and regulation of genome editing.

What's the potential of genome editing for muscle-wasting conditions?

As many muscle-wasting conditions are genetic, in other words they are caused by a mutation in a gene, they could potentially be treated with genome editing. Researchers around the world are looking into this for several muscle-wasting conditions, including:

- Duchenne muscular dystrophy
- congenital muscular dystrophy
- facioscapulohumeral muscular dystrophy
- myotonic dystrophy
- limb girdle muscular dystrophy and
- mitochondrial disease.

A recent study by researchers in the UK and USA showed that a CRISPR/Cas9 therapy could correct the dystrophin gene in a dog model of Duchenne muscular dystrophy. This boosted dystrophin production in the dogs' muscles, heart and diaphragm. The muscles also appeared healthier, but we don't know how functional they were as the researchers didn't assess this.

While these results are promising, the study was too small and too short to know whether the CRISPR/Cas9 therapy was safe and effective. It's important that larger, longer-term studies are carried out.

When will it be available?

Although there have been some promising advances recently, there's still a lot we don't know about the safety of genome editing. A lot more research is needed before the technique can be trialled in people with muscle-wasting conditions. It's difficult to estimate how long this might take, but it's hoped that we can learn from advances in research into other conditions along the way. There are currently genome editing therapies in early clinical trials for several conditions, including beta-thalassemia, sickle cell disease and some types of cancer.

What genome editing research is MDUK supporting?

MDUK currently funds two genome editing research projects:

1. Genome editing to repair duplications in Duchenne muscular dystrophy

Professor Francesco Muntoni at University College London is investigating whether duplication mutations causing Duchenne muscular dystrophy can be corrected using genome editing.

His team have designed a CRISPR/Cas9 system, which has been packaged into a type of virus called a 'lentivirus'. They are currently testing this in cells from a patient, to see whether it can remove the duplicated DNA and restore dystrophin production. This project is co-funded with Duchenne UK and is currently in its final year.

2. Developing genetic therapies for Duchenne muscular dystrophy

As part of her MDUK Lectureship, Dr Linda Popplewell at Royal Holloway University is also investigating genome editing strategies for Duchenne muscular dystrophy. Her team have designed CRISPR/Cas9 systems to correct different dystrophin mutations and to switch off genes involved in muscle scarring (fibrosis).

The overarching goal is to combine these two systems into a single treatment that can boost dystrophin production and halt the fibrosis. Dr Popplewell is currently in the fourth year of her five-year Lectureship.

To find out more contact Jenny Sharpe
j.sharpe@musculardystrophyuk.org
or call 020 7803 2885.

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The road to treatment

The development of drugs and treatments generally takes place in three successive stages: basic research, preclinical research and clinical studies. Each of these stages can take many years to complete. And even if the therapy doesn't make it out of the lab to patients, scientists are learning a lot along the way. What doesn't work can often tell us as much as what does work.

Here we describe what happens in each stage, the next and final steps to treatments, and how MDUK is supporting this process.

Basic research

This focuses primarily on understanding the cause of a condition and how this leads to muscle weakness and wasting. It usually takes place in the lab and involves studying cells – which could be from patient samples – and animal models (animals that have a similar condition to the one the team is focusing on).

Once researchers understand more about the cause of a condition, they can start to investigate possible ways to address this, and tackle the muscle problems and other symptoms. At this point, the research starts to become 'translational', meaning researchers use the findings from the basic lab studies to develop targeted potential treatments. They then further assess them in preclinical studies.

Preclinical research

This stage involves all the experiments to assess the safety and efficacy of a treatment before testing it in human trials. The tests will be carried out in cell and animal models.

The treatment is also tested in healthy animals, in what are known as toxicology studies. These help scientists identify harmful side-effects, and establish the safest dosing range to use in clinical trials.

Clinical studies and support

This stage covers any form of research involving people. The research includes observational studies, to understand more about a muscle-wasting condition and how it progresses (its natural history), and clinical trials, to assess the safety and effectiveness of specific interventions. These interventions could be medical products, for example, drugs, devices, vaccinations; medical procedures, such as a type of surgery; or changes to a person's lifestyle, such as an exercise regime.

In order for clinical trials to take place, certain types of clinical support and infrastructure must be available. These include clinical trial co-ordinator roles, to help with the setting up and running of clinical studies at a particular centre. Patient registries are also valuable resources as they provide access to patients who might benefit from taking part in clinical trials.

Licensing and reimbursement

After a new treatment has gone successfully through the lengthy process of clinical trials, there is still the final hurdle of making it available to patients in the UK. The treatment must be approved by the European Medicines Agency (EMA), and then by the relevant health technology assessment (HTA) bodies. In the UK these are the National Institute for Health and Clinical Excellence (NICE) and the Scottish Medicines Consortium (SMC). Guidance published by NICE will apply to England but is usually followed by Wales and Northern Ireland as well. While EMA evaluates a drug's benefits and risks, the HTA bodies assess whether it should be funded (or reimbursed) by the NHS.

When you're living with a muscle-wasting condition, we know that every day counts. That's why we're pressing hard to get effective treatments to people faster. We'll work with other charities, and with individuals and families, to ensure a more effective, open drug approval process for rare diseases.

We'll do this by pressing regulation and reimbursement bodies throughout the UK to improve their approach to assessing and delivering rare disease treatments so that treatments will be available to all people who could benefit from them.

How does MDUK support clinical trials?

Clinical trials are an important step in the research process. We want to ensure everyone has the opportunity to be involved in a clinical trial if they wish.

While the number of clinical trials taking place in the UK is growing, there aren't enough sites that have the staff and the infrastructure required to carry out these clinical trials. We're helping to meet the growing demand for clinical trials through our investment in the MDUK Oxford University Neuromuscular Centre, which promotes the translation of scientific research into clinical trials. You can read more about this on p16.

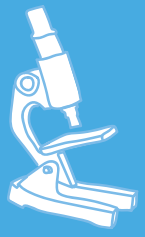
We're also funding two clinical trial co-ordinator posts and pressing for more staff at other neuromuscular centres UK-wide to grow capacity to deliver trials and treatments. We want to see more children and adults with muscle-wasting conditions being able to take part in clinical trials so that ultimately people can access potential treatments much sooner.

To find out more about what clinical trials are taking place in the UK, do get in touch with our Research Line on research@musculardystrophyuk.org or 020 7803 4813

MDUK's research programme

13 Basic research

- 4 Congenital myopathy
- 2 Duchenne and Becker muscular dystrophy
- 1 Emery Dreifuss muscular dystrophy
- 1 Limb girdle muscular dystrophy
- 1 LMNA congenital muscular dystrophy
- 2 Myotonic dystrophy
- 1 Nemaline myopathy
- 1 Neuropathies



22 Preclinical research

- 2 Collagen VI-related myopathy
- 10 Duchenne and Becker muscular dystrophy
- 3 Duchenne muscular dystrophy
- 2 Facioscapulohumeral muscular dystrophy
- 2 Myotonic dystrophy
- 1 Nemaline myopathy
- 2 Spinal muscular atrophy

The numbers indicate the number of projects in progress relating to specific conditions.

See p12-14 for more information about where these research projects are taking place. You can also read more detailed project summaries on our website:
www.musculardystrophyuk.org/progress-in-research/research-projects

19 Clinical studies and support

- 4 All
- 1 Collagen VI-related myopathy
- 7 Duchenne muscular dystrophy
- 1 Facioscapulohumeral muscular dystrophy
- 2 Myotonic dystrophy
- 1 Myotubular myopathy and centronuclear myopathies
- 1 Neuropathies
- 2 Spinal muscular atrophy

Access to treatments

We continue to work with families, clinicians, decision makers and companies through our FastTrack campaign to fight for access to new treatments.

We are collaborating with other patient organisations to improve the way rare disease treatments are assessed and delivered by the NHS.

We have colour-coded the different research stages so you can quickly identify the current status of each MDUK-funded project.

To find out more or to get involved in our FastTrack to treatments campaign, get in touch with Clare Lucas c.lucas@musculardystrophyuk.org or call 020 7803 4838.

Our research grants

Basic research **Preclinical research** **Clinical studies and support**

All conditions

Oxford Neuromuscular Translational Research Centre	Prof Matthew Wood	University of Oxford	Ongoing
Clinical trial co-ordinator (Newcastle)	Dr Michela Guglieri	University of Newcastle	Ongoing
Clinical trial co-ordinator (London)	Prof Francesco Muntoni	University College London	Ongoing
Evaluating a self-management programme for people with neuromuscular conditions	Dr Gita Ramdharry	University College London	2018-2022

Collagen VI-related myopathies

Developing molecular patches for the treatment of collagen VI-related conditions	Prof Francesco Muntoni	University College London	2017-2020
Making a mouse model with Ullrich congenital muscular dystrophy and testing a potential treatment	Prof Carsten Bönnemann	National Institute of Neurological Disorders and Stroke, NIH, USA	2017-2019
Facilitating clinical trials for collagen VI-related conditions	Prof Volker Straub	University of Newcastle	2016-2019

Congenital muscular dystrophies and myopathies

Understanding the role of KY protein in muscle	Dr Gonzalo Blanco	University of York	2018-2020
Investigating the role of INPP5K in congenital muscular dystrophy	Dr Laura Swan	University of Liverpool	2018-2021
Finding new genes associated with congenital muscular dystrophies and congenital myopathies	Prof Francesco Muntoni	University College London	2018-2020
Understanding the molecular causes of myosin-related congenital myopathies	Dr Julien Ochala	King's College London	2017-2021

Duchenne muscular dystrophy

Improving muscle repair in Duchenne muscular dystrophy	Prof Henry Houlden	University College London	2018-2019
Making 'mini-muscles' to test potential treatments for Duchenne muscular dystrophy	Dr Francesco Saverio Tedesco	University College London	2017-2021
Investigating the effect of Duchenne muscular dystrophy on bone development	Dr Claire Wood	University of Edinburgh	2016-2020
NorthStar database	Dr Adnan Manzur and Prof Francesco Muntoni	University College London	Ongoing
Using novel MRI techniques to study changes in bone health in Duchenne muscular dystrophy	Dr Jarod Sze Choong Wong	University of Glasgow	2017-2018
Investigating the effect of Duchenne muscular dystrophy on the brain	Prof Volker Straub	University of Newcastle	2015-2018

Basic research | Preclinical research | Clinical studies and support

Studying bone health in boys with Duchenne muscular dystrophy – extension study	Dr Anne-Marie Childs	University of Leeds	2017-2018
Improving care for adults with Duchenne muscular dystrophy	Dr Ros Quinlivan	University College London	2017-2021
Studying bone health in boys with Duchenne muscular dystrophy	Dr Shuko Joseph	University of Glasgow	2015-2018
Universal Microdystrophin Gene Therapy Clinical Trial for Duchenne Muscular Dystrophy (UNITE-DMD)	Prof George Dickson, Prof Francesco Muntoni and Prof Volker Straub	Royal Holloway University, Unviersity College London and University of Newcastle	2017-2021

Duchenne/Becker muscular dystrophy

Predicting the impact of exon skipping on dystrophin function	Dr Federica Montanaro	University College London	2016-2018
Understanding the effects of Duchenne muscular dystrophy on heart function to improve gene therapy	Prof Jennifer Morgan	University College London	2017-2021
Reducing muscle scarring in Duchenne muscular dystrophy	Dr Linda Popplewell	Royal Holloway University	2017-2021
Assessing the feasibility of a new cell- and gene-based therapy for Duchenne muscular dystrophy	Prof Jennifer Morgan	University College London	2017-2020
Is the activation of AMPK a potential treatment of Duchenne muscular dystrophy?	Prof Dominic Wells	Royal Veterinary College	2017-2018
Identifying small molecules for Duchenne muscular dystrophy	Prof Kay Davies	University of Oxford	2016-2019
Developing a cell and gene-based therapy for Duchenne muscular dystrophy	Dr Francesco Saverio Tedesco	University College London	2015-2019
Assessing muscle fibrosis by MRI	Prof Volker Straub	University of Newcastle	2017-2018
Genome editing to repair duplications in Duchenne muscular dystrophy	Prof Francesco Muntoni	University College London	2016-2018
Developing genetic therapies for Duchenne muscular dystrophy	Dr Linda Popplewell	Royal Holloway University	2015-2020
Discovering biomarkers for Duchenne muscular dystrophy	Prof Matthew Wood	University of Oxford	2014-2018
Moving closer to a gene therapy for Duchenne muscular dystrophy	Prof George Dickson	Royal Holloway University	2015-2018
Using molecular patches to prevent heart muscle disease in Duchenne muscular dystrophy	Prof Matthew Wood	University of Oxford	2016-2019

Emery-Dreifuss muscular dystrophy

Understanding the causes of Emery-Dreifuss muscular dystrophy	Prof Eric Schirmer	University of Edinburgh	2018-2020

Facioscapulohumeral muscular dystrophy (FSHD)

Understanding how DUX4 affects muscle regeneration in FSHD	Dr Robert Knight	King's College London	2017-2021

Basic research | Preclinical research | Clinical studies and support

Development of molecular patches for the treatment of facioscapulohumeral muscular dystrophy	Dr Linda Popplewell	Royal Holloway University	2016-2019
FSHD registry	Prof Hanns Lochmüller	University of Newcastle	Ongoing

Limb girdle muscular dystrophy

Finding new genes that cause limb girdle muscular dystrophies	Prof Volker Straub	University of Newcastle	2017-2018

LMNA congenital muscular dystrophy

Understanding the variable clinical severity of LMNA-CMD	Gisèle Bonne	Institute of Myology, France	2018-2020

Myotonic dystrophy

Understanding the nuclear changes that lead to myotonic dystrophy type 1	Dr Judith Sleeman	University of St Andrews	2016-2019
Understanding the genetics of myotonic dystrophy type 1	Prof Darren Monckton	University of Glasgow	2015-2019
Developing tools to identify effective treatments for myotonic dystrophy	Prof J David Brook	University of Nottingham	2017-2018
Developing an advanced molecular patch therapy for myotonic dystrophy type 1	Prof Matthew Wood	University of Oxford	2017-2020
Validating clinical measures for monitoring the progression of myotonic dystrophy type 1	Dr Paul Maddison	University of Nottingham	2017-2020
UK myotonic dystrophy registry	Dr Michaela Guglieri	University of Newcastle	Ongoing

Myotubular and centronuclear myopathy

Myotubular and centronuclear myopathies registry	Prof Hanns Lochmüller	University of Newcastle	Ongoing

Nemaline myopathy

Improving the diagnosis of nebulin-based nemaline myopathy	Dr Carina Wallgren-Pettersson	University of Helsinki	2017-2020
Putting the brakes on muscle atrophy in nebulin-based nemaline myopathy	Dr Coen Ottenheijm	VU University Medical Centre, Amsterdam	2017-2020

Spinal muscular atrophy

Could an existing drug be a treatment for spinal muscular atrophy?	Dr Melissa Bowerman	Keele University	2018-2022
Developing a genetic therapy for spinal muscular atrophy	Prof Matthew Wood	University of Oxford	2014-2018
Developing an MRI technique for monitoring spinal muscular atrophy	Prof Andrew Blamire	Newcastle University	2018-2021
Improving standards of care and facilitating clinical trials for spinal muscular atrophy (SMA-REACH UK)	Prof Francesco Muntoni	University College London	2016-2018

To find out more about these research projects, please get in touch with our Research Line at research@musculardystrophyuk.org or 020 7803 4813

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Progress on our major research projects

Bringing treatments to people more quickly

While there's really exciting neuromuscular research happening here in the UK, centres across the country can't keep up with the increase in demand for clinical trials, owing to a lack of capacity and resources. That's why we've partnered with the University of Oxford to establish the MDUK Oxford University Neuromuscular Centre – a major centre for neuromuscular research and clinical trials.

This Centre in Oxford complements significant investment in research and clinical trials in Newcastle and London, and builds on Oxford's world-leading research and expertise in neuromuscular conditions. This third centre will be a game changer for individuals and families living with muscle-wasting conditions in the UK by enabling more potential treatments to be tested in clinical trials. The new resources include start-up seed funding for research costs for clinical lecturers as well as a number of new staff posts.

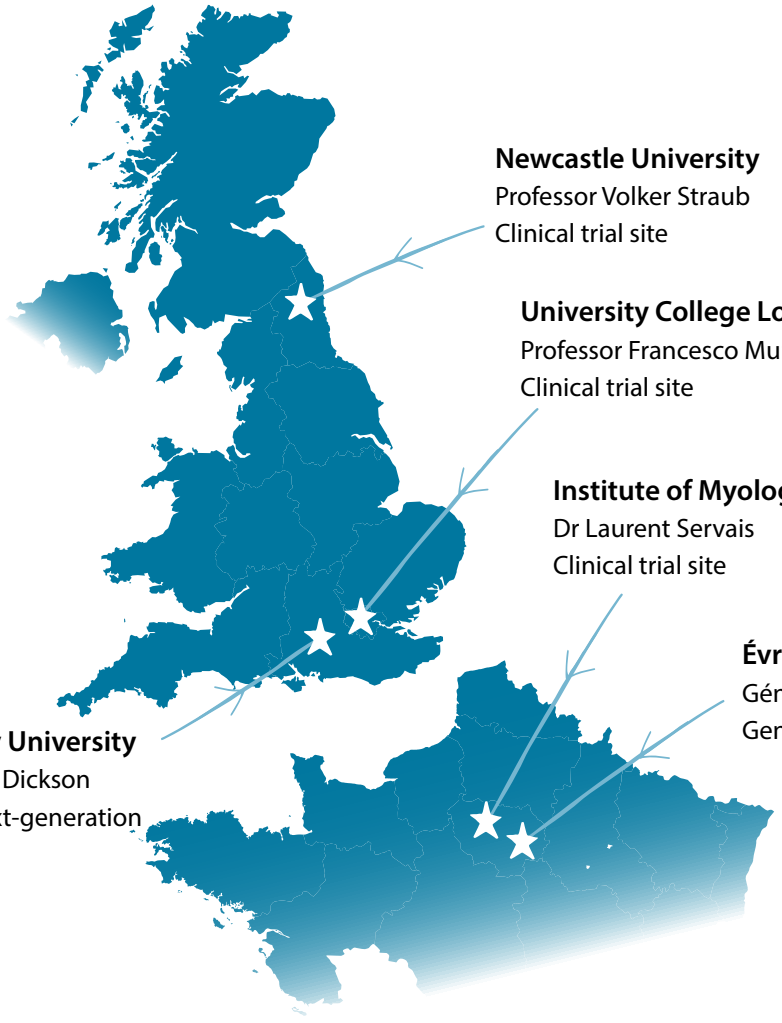
Recruitment for the 'Chair' to oversee the Centre is currently underway. We're looking for a distinguished clinician with a wealth of knowledge and experience in running clinical trials. We hope that the Chair will be in post by the start of the new academic year.

A Project Manager is in post, to help with administration at the Centre. They will have a key role in co-ordinating activities between the three academic departments (Department of Physiology, Anatomy and Genetics, Department of Paediatrics, and the Nuffield Department of Clinical Neurosciences) and the hospital (Oxford University Hospitals NHS Foundation Trust).

Professor Matthew Wood, Director of the MDUK Oxford University Neuromuscular Centre

Photo © Suki Mok

International collaboration



Newcastle University
Professor Volker Straub
Clinical trial site

University College London
Professor Francesco Muntoni
Clinical trial site

Institute of Myology, Paris
Dr Laurent Servais
Clinical trial site

Évry, Paris
Généthon
Gene therapy manufacture

Royal Holloway University
Professor George Dickson
Research into next-generation therapies

Facilitating drug development

As a long-standing supporter of research into gene therapy, MDUK is delighted to be taking a bold step and testing its safety in people living with muscle-wasting conditions. UNITE-DMD is a four-year international effort to develop and test a gene therapy for Duchenne muscular dystrophy in an early phase clinical trial.

This is an excellent example of collaboration, bringing together teams of researchers from the UK and France, who are working on different parts of the project (see map).

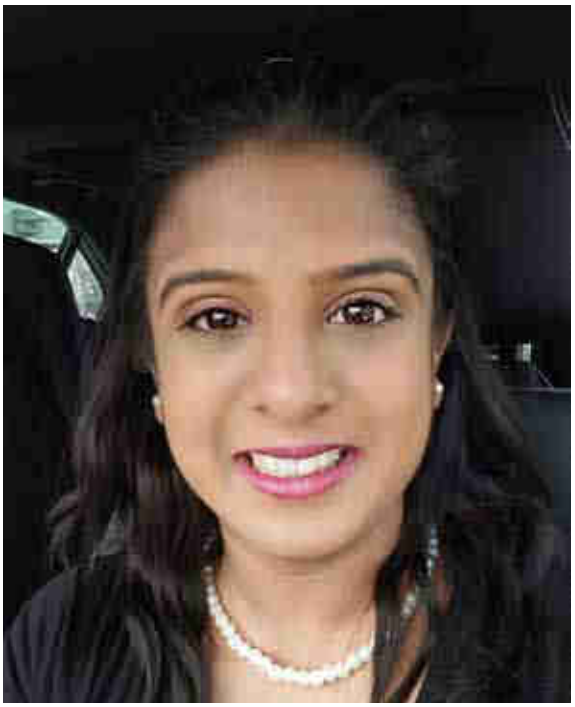
Work has begun in Professor George Dickson's lab to refine the gene therapy; the aim is to ensure a pipeline of improved gene therapy products. Preparatory work for the clinical trial is also underway with Professor Francesco Muntoni and Professor Volker Straub, at London and Newcastle respectively, currently recruiting the clinical staff to run and oversee the trial.

Production of the gene therapy is also progressing. The product needs to be manufactured in large enough amounts and to a high enough quality to be used in the clinical trial. This work is being funded and carried out by our French partners AFM and Généthon, and forms an essential part of the UNITE-DMD project.

Behind the scenes of a clinical trial

Clinical trial co-ordinators play an important role in the successful running of clinical trials. So much so that drug companies are unlikely to select a hospital to run a trial if a clinical trial co-ordinator is not in post. We understand the importance of clinical trials, and we want to ensure more children and adults with muscle-wasting conditions can take part in clinical trials, so we're currently funding two clinical trial co-ordinator posts.

Meet Hinal Patel (pictured), a senior clinical trial co-ordinator from the Dubowitz Neuromuscular Centre at Great Ormond Street Hospital (GOSH), who talks about her role.



Can you tell us a bit about yourself and your role?

From a young age, I have always enjoyed learning about science and, after completing my Master's degree in Cancer Therapeutics, I knew I wanted to work in a clinical research environment. Initially, I worked at Queen Mary's University helping to co-ordinate cancer trials before moving to this MDUK-funded clinical trial co-ordinator position at GOSH in 2011. As a trials co-ordinator, I help with the setting up and running of neuromuscular clinical trials at the hospital. This involves a range of tasks such as trial administration, informing clinical staff about trial protocols as well as organising participant travel.

What's involved in setting up a clinical trial and how long does it take?

Setting up a clinical trial in the UK can be a lengthy process as it involves many stages. Firstly, a drug company needs to decide which hospital(s), or clinical study site(s), will run the trial. To be selected, the hospital needs to complete a questionnaire to show it has the right resources to successfully conduct the trial (for example, research staff, patient population and facilities). The speed of this selection process depends on the drug company; it can be as quick as two months but may take longer. Once selected, the hospital then needs to get approval from different regulatory bodies, such as ethics committees, Medicines and Healthcare products Regulation Agency (MHRA), Health Research Authority (HRA) and others as required. They make sure the trial is safe, well planned and in the patients' best interest. In addition, all staff working on the trial need to be trained so that they know what the study protocol involves and what is expected from them. From my experience, once a hospital is selected to run a trial, it usually takes six to nine months before patient recruitment can start.

Can anyone take part in a clinical trial taking place in the UK?

Yes, regardless of where you live in the UK, you can take part in a trial as long as you are registered to a GP, have an NHS number and meet the eligibility criteria of the trial. The eligibility criteria will vary from study to study;

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you can find out about a trial's eligibility criteria on clinicaltrials.gov or through the MDUK Research Line (contact details at the end of the article). You can also speak to your doctor to find out if you meet the criteria for a particular trial.

Do you have to pay any costs when participating in a trial?

Any travel, refreshments and accommodation (if required) costs are paid for. The way these expenses are paid can vary depending on the study. For some trials, participants are required to pay for their expenses first and then they will be reimbursed. For other studies, we can pre-book travel and accommodation. Before starting a trial, participants are told how the expenses during the study will be paid for.

Is it possible for a UK resident to take part in an international trial?

Every country has its own guidelines regarding trial recruitment, so it's difficult to say if a UK resident would be eligible to participate in an international trial. I would recommend getting in contact with the trial's clinical study site for further information on their trial recruitment policy.

If someone has previously taken part in a trial, can they take part in another one?

Individuals can usually take part in another study but they may have to wait a certain period between trials. This is known as the 'wash-out period' and usually is three to six months. This is to make sure an experimental drug is completely removed from the body before taking another one.

However, at the moment, individuals that take part in a gene therapy study (when a virus is used to replace or modify a gene) may not be able to take part in future trials. This is because it is not known how long it takes for the virus to leave the body and is therefore difficult to define the wash-out period.

What advice would you give to individuals interested in taking part in clinical trials?

I would recommend speaking to your neuromuscular consultant/nurse and signing up to your condition-specific registry. At GOSH, we recruit participants for clinical trials from our research database. We select trial participants (who meet the eligibility criteria) in the order they were added, essentially a first come, first served approach. Anyone in the UK with a neuromuscular condition can go onto our database, by contacting me (hinal.patel@ucl.ac.uk) or our senior research nurse, Katie Groves (Katie.groves@gosh.nhs.uk).

If you have any questions about clinical trials or research into your condition, please get in touch with the MDUK Research Line on 020 7803 4813 or research@musculardystrophyuk.org

Muscular Dystrophy UK
Fighting muscle-wasting conditions

"We're here for everyone and there's no such thing as a silly question."

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This is an exciting time for research. Every day, scientists are finding out more about muscle-wasting conditions, so we can bring new treatments and new hope to everyone affected.

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GET INVOLVED:
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PREFER: giving patients a voice in drug development

prefer.
PATIENT PREFERENCES

In our commitment to giving patients a voice in drug development, Muscular Dystrophy UK is working with pharmaceutical companies, academics, patients, healthy technology assessment bodies and regulatory authorities in a five-year international project called PREFER.

A drug goes through several stages in its 'life cycle'. The PREFER project will find out when and how patient preferences should be incorporated into this cycle.

Drugs are developed for patients, so it is essential that their views and preferences be incorporated into the drug life cycle (see figure above). For example, pharmaceutical companies need to know what patients value in order to develop drugs that are suitable for patients' needs.

Regulatory agencies also need to understand patients' preferences, so that they can make informed decisions on whether to make new drugs available. Similarly, patient preference information is helpful to health technology assessment (HTA) bodies, who decide whether drugs should be funded by healthcare systems such as the NHS.

A study collecting this sort of information is called a 'patient preference study'. At the moment, there is little guidance on the use of these studies during the drug life cycle. The PREFER project will address this by producing evidence-based recommendations. These will advise on how patients' preferences should be collected and how this information should be used by decision-makers.

Since the project started in 2016, the PREFER team have spent a lot of time studying the different ways of collecting patient preferences. These methods have been reviewed and some are now going to be assessed in patient preference studies in three clinical areas: rheumatoid arthritis, cancer and neuromuscular conditions.

Muscular Dystrophy UK is helping to lead the neuromuscular patient preference study together with Newcastle University. The study will focus on myotonic dystrophy type 1 and mitochondrial disease. We are interested to know what adults with these conditions and their caregivers think about different treatments (real treatments and hypothetical ones) and what trade-offs[1] they are willing to make. This information will help pharmaceutical companies to design more patient-centric treatments and clinical trials.

The study will consist of two parts:

1. interviews and focus groups (March – April 2019)
2. online survey (September - December 2019).

[1] A trade-off is the act of balancing a negative against a positive, for example the side-effects or risk of a treatment against the benefits.

If you're interested in being interviewed or taking part in a focus group, please get in touch with Dr Cecilia Jimenez-Moreno (Cecilia.Jimenez-Moreno@newcastle.ac.uk).

We'll also post more information about the study on our website soon.

If you'd like further information about the PREFER project, please get in touch with our Research team at research@musculardystrophyuk.org Or visit the PREFER website: www.imi-prefer.eu

"The PREFER project is a great opportunity to increase the awareness of the unmet needs of muscle-wasting conditions. We hope to capture the interest of industry partners and regulatory bodies to push for further research in these diseases."
Dr Cecilia Jimenez-Moreno,
Newcastle University

Members of the PREFER consortium at the 2018 annual meeting in Leuven, Belgium

Disclaimer: This news item and its contents reflects the PREFER project's view and not the view of IMI, the European Union or EFPIA.

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