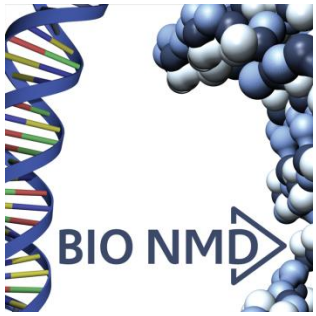
ISSUE 1 SEPTEMBER 2010

BIO-NMD newsletter



Inside This Issue

Send us your feedback via:
www.bio-nmd.eu/forPatients/
or email:
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Welcome!

Welcome to the first BIO-NMD patient-focused newsletter. Whether this is the first time you have read about BIO-NMD, or whether you are already familiar with the project, we hope that you will find the information here of use and interest.

As this is the first edition, it contains a general overview and explanation of what BIO-NMD is doing as well as who is involved, a diary of events and other news from related projects and organisations. You will also find a topical main article about an important issue for everyone involved in medical research whether as a patient, a clinician or a research scientist – this issue focuses on the ethical issues in biobanking.

Any comments or feedback you have about this newsletter would be most appreciated – please let us know what is useful, what is not and what you feel is missing so that we can improve the next edition (probably in around 9 months time).

Thank you for your interest in BIO-NMD!

Cathy Turner,

Communication and Dissemination Officer, BIO-NMD
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What is BIO-NMD?

BIO-NMD is a 3 year EU-funded research project focusing on Duchenne and Becker muscular dystrophies and collagen VI-related myopathies (which includes Ullrich congential muscular dystrophy and Bethlem myopathy). It is closely linked to the TREAT-NMD network of excellence and was borne from collaborations and research ideas within that network.

Visit the project's website at

www.bio-nmd.eu

The project is searching for 'biomarkers' in people with these conditions. Biomarkers are substances in the body that offer a way to measure normal or abnormal processes.

A major application of new biomarkers is in clinical trials. At the moment, when a new drug is being tested, researchers use a variety of ways to measure whether the drug has had a positive effect. However, these measures are not always very good at showing small changes and improvements in a patient's symptoms, especially when the drugs are only being tested for a short time.

However, if the BIO-NMD project can find biomarkers in patients' blood or urine, samples of these can be taken throughout clinical trials. Measuring the levels of these biomarkers will show researchers clearly and accurately whether the drug being tested has had an effect or not.

Biomarkers offer a way to measure processes in the body

There will be other benefits in discovering biomarkers for neuromuscular diseases:

- Blood and urine testing may be able to replace the use of muscle biopsies
- Diagnosis can happen earlier because testing for biomarkers is quicker and easier than genetic testing
- Disease progression can be accurately measured allowing better clinical management of symptoms
- Existing treatments (including drug dosage) can be adjusted to precisely meet the needs of individual patients to ensure they get the maximum benefit

Who is involved in BIO-NMD?

Professor Alessandra Ferlini at the University of Ferrara coordinates the project

For projects like this to be successful, the collaboration of many professionals with different skills is required. There are 12 European partners involved in the BIO-NMD project coordinated by Professor Ferlini at the University of Ferrara, Italy. For example, some are well placed to collect and distribute patient samples and others are experts in studying genes or proteins, data analysis, animal models or project management. There is also a Patient Association Committee whose job it is to make sure patients' interests are represented and that they are kept informed about BIO-NMD's progress. The project's website has full details about the 12 partners and the patients' committee at **www.bio-nmd.eu**

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The BIO-NMD website

BIO-NMD's website contains more information for patients

BIO-NMD has its own website (www.bio-nmd.eu) which has full details of the project, progress updates and information about who is involved. There is also more information for patients produced with the kind help of the Muscular Dystrophy Campaign and currently translated into French, Italian and Dutch – hopefully more languages to follow.

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Information For Patients

What is the BIO-NMD project?

BIO-NMD is an EU funded research project focusing on Duchenne and Becker muscular dystrophies and collagen VI-related myopathies (which includes Ullrich congential muscular dystrophy and Bethlem myopathy).

The project is searching for 'biomarkers' in people with these conditions. Biomarkers are substances in the body that offer a way to measure normal or abnormal processes in the body. This means that processes associated with particular diseases can be measured and disease progression monitored. It also means that the effect of drugs or other therapies on disease progression can be evaluated.

A biomarker may be a protein found in bodily fluids such as the blood or urine, or in tissues such as the muscles. Alternatively, a particular gene could be a biomarker. Different genes in our DNA are switched on and off as processes occur in the body, and measuring the activity of certain genes may be able to give an accurate picture of disease progression.

Where available, this search for biomarkers will use human blood, urine and muscle samples already stored in repositories called 'BioBanks'. New samples will be collected from patients if needed.

How might this benefit patients?

This research aims to improve the development of treatments and diagnosis of people affected by neuromuscular disease.

A major application of new biomarkers is in clinical trials. At the moment, when a new drug is being tested, researchers use a variety of ways to measure whether the drug has had a positive effect. One measurement used is the 6 minute walk test. However, these measures are not always very good at showing small changes and improvements in a patient's symptoms, especially when the drugs are only being tested for a short time.

However, if the BIO-NMD project can find biomarkers in patients' blood or urine, samples of these can be taken throughout clinical trials. Measuring the levels of these biomarkers will show researchers clearly and accurately whether the drug being tested has had an effect or not.

Other benefits of biomarkers include:
• Blood and urine testing may be able to replace the use of painful and invasive muscle biopsies in the future
• Diagnosis can happen earlier because testing for biomarkers is quicker and easier than genetic testing
• Disease progression can be accurately measured allowing better clinical management of symptoms
• Existing treatments (including drug dosage) can be adjusted to precisely meet the needs of individual patients to ensure they get the maximum benefit.

Why have Duchenne and Becker muscular dystrophies and collagen VI-related myopathies been chosen for the study?

Links
Cure CMD
Fondazione Telethon
Muscular Dystrophy Campaign
United Parent Projects Muscular Dystrophy

Main Article – The Ethics of Biobanking

Introduction

Biobanks are collections of human biological samples which may be used for research including cells, body fluids (such as plasma), tissues (such as muscle biopsies) and DNA. These samples are linked to information about the individual who provided them, for example their lifestyle, gender, age and medical information. It is this information which makes the samples especially useful for medical research.

Samples may be collected from patients in clinics or during surgical procedures, from healthy volunteers and during post-mortems. Permission is required from the patients (or their families where appropriate) before samples can be taken, stored and used by biobanks. This article aims to discuss the use of biobanks, especially in relation to neuromuscular disease, and some of the ethical issues which must be considered. It focuses on UK practice.

Why do we need biobanks?

When researchers are trying to find out more about a disease or develop a new drug treatment they need human volunteers with that disease to study. They usually need to look at samples of biological material to find out how a disease progresses or how a new drug affects the body. Often it is just not practical to ask those volunteers to come into a clinic to have samples taken, particularly if the disease being studied is a rare one (which affects less than 1 in 2000 people)[1] – because to have enough volunteers, people may need to travel hundreds of miles.

However, biobanks encourage the storage of biomaterials and give researchers access to the samples they need from patients over a very wide geographical area.

The basic scientific research being carried out on neuromuscular diseases (NMDs) relies on the availability of high-quality biomaterials. For example, testing potential new drugs using the cells of people with NMDs helps to determine whether those drugs may be effective against that disease.

Some examples of biobanks:
EuroBioBank, established in 2001, is a network of 15 separate biobanks across Europe which is dedicated to supporting research into rare diseases including neuromuscular disease. Its mission is to create a collection of material large enough to be useful and to allow the exchange of biological material in order to help speed up research. Samples of DNA as well as tissue are provided for selected research projects, the results of which often result in scientific publications listed on the EuroBioBank website.[2] The network is coordinated by the European Organisation for Rare Diseases (Eurordis).

The EuroBioBank is an example of a 'retrospective' resource, collecting information and samples from people who have already developed a particular disease or who have a family history of a condition.[3]

Another example is the UK Biobank.[4] This is a 'prospective biobank'[3] meaning it collects samples from healthy volunteers and will follow their health over the coming years. DNA but not tissue is stored. More than 500,000 people between the ages of 40-69 in the UK have so far donated samples. By giving permission for researchers to find out about their current health and lifestyles, study and store samples of their blood, urine and saliva and follow their health records, the volunteers may play a crucial role in research into the prevention and treatment of many diseases – mainly common diseases - in the future.[4]

Biobanks and BIO-NMD:
BIO-NMD is a research project which is looking for biomarkers in patients with neuromuscular disease. A biomarker is a substance in the body that allows scientists to measure how a disease is progressing or what effect a drug is having. A biomarker may be a protein found in bodily fluids such as the blood or urine, or in tissues such as the muscles. Alternatively, a particular gene could be a biomarker.[5]

This search for biomarkers will require samples from patients with the NMDs under study as well as some healthy control samples. Biobanks will be an important source for these samples. For example, if the team wanted to compare blood samples of boys with Duchenne Muscular Dystrophy who stopped walking earlier than expected with those who continued to walk for longer than expected, they can request those samples from a biobank.

Whilst invaluable to research, such large collections of biological material and associated personal, sensitive data about the patients from which they came has many ethical implications which need careful consideration by all concerned.

BIO-NMD plans to use EuroBiobank resources (http://dev.eurobiobank.org/index.html) which are governed by the ethical guidelines detailed below. Samples collected in other ways by the project, for example directly from patients, will also be covered by these guidelines.

The Ethical Issues

Informed consent:
In the 1990s there was a national scandal in the UK when it was revealed that some hospitals had routinely removed tissues and organs from children during surgical procedures and post-mortem examinations.[6] This biomaterial was stored by the hospitals for use in research often without the knowledge of the children's parents. In many cases, parents had signed a consent form to allow the post-mortem but had not realised that this also gave permission for tissues and organs to be retained for research purposes.

In 2006, the Human Tissue Act[7] came into force, largely in response to the events of the 1990s. The Act lays down very clear rules for those dealing with human cells, tissue and organs. Every effort must be made to obtain informed consent before the removal, storage or use of human biomaterials. Donors and their families should be made aware of the expected or likely use of their material – they should be 'informed' about what they are agreeing to.[8] Importantly, donors are usually asked whether they will also permit any surplus material from their sample to be used for further research projects in the future.

Whilst the Human Tissue Act applies in the UK, the rest of Europe is also covered by similarly strict rules covering the collection, storage and use of human biomaterials.

Payment:
In some countries payment is offered for human samples, and whilst this can increase donations, for example of blood to blood banks, it can also cause problems with the quality of the donated blood.

In the UK and in many other countries, it is not usual for volunteers and patients to be paid for their donation. Although it is not illegal or necessarily unethical there is a wide belief that donations should be given freely, for the potential benefit of wider society through improved medical health or for others who have similar health problems to patient donors.

Data protection:
In order for biomaterials in biobanks to be useful to researchers, they must be linked to certain details about the donor. However, it is also important that the donor's identity is kept confidential partly in order that medical information which may be used by third parties such as life insurance companies or employers is not revealed. The consent form which is signed makes clear to the donor that the sample will be anonymous but will be linked to their medical data and made available to researchers. The only person who can ever link the sample with the individual is the donor's doctor or the curator of the biobank. It is never possible for the researchers using the samples or any other third parties to know the identity of the person who gave that sample.

Ownership:
Many people who donate samples to biobanks want to know who owns their material. Patients retain control over the use of their data because in most cases they can request that their tissue be destroyed and their record deleted. However, to talk about 'ownership' of biological material may be misleading. This is because any commercial gain made as a result of using biomaterial remains that of the biobank – the patient has no claim on a share of any profit made from growing a cell line for example.

Feedback to patients:
There is the potential that research using samples may uncover significant information about the health of a donor. This may be information about a pre-existing condition or about something previously unknown. What should be done, for example, if genetic testing reveals that a donor is carrying a mutation which puts them or members of their family at a higher risk of developing a potentially treatable condition later in life? Should a patient who donated a sample for research into heart disease be told if it is discovered that they are likely to develop breast cancer?

Some countries within the EuroBiobank ask patients specifically whether they wish to be informed of research results. It is hoped that there will be standardisation on this across all members in the future. This is where it becomes important that the doctor or curator can re-link a donor's sample with their identity - although this is still never revealed to anyone else.

The UK Biobank – a much larger repository, explicitly states that donors will not be informed of medically significant information arising from their samples. Because of these differences, it is important for potential donors to understand the conditions attached to their donation and to discuss any concerns they may have with their doctor.

People who donate samples to biobanks may receive feedback and benefit in other ways too – for example, the outcomes of research can be made accessible to them along with information about the development of new treatments.

Conclusion

Biobanks are making an important contribution to medical research. Increasing investment is being made into establishing these important repositories of information. For example, Germany has recently announced plans for a €210 million project which will collect samples from 200,000 donors along with scans of the brain, heart and other organs of 40,000 of the subjects, using magnetic resonance imaging.[9] As more information about patients/donors is held, tight regulation of the use of this data becomes more important than ever. In order for biobanking to be useful, donors must be willing to participate. They must therefore feel confident that their own interests are protected and that rigorous ethical guidelines have been followed.

Websites used (last accessed 16 August 2010)

1. http://www.eurordis.org/about-rare-diseases
2. http://www.eurobiobank.org/en/information/info_institut.htm#objectives
3. http://genome.wellcome.ac.uk/doc_WTX036455.html
4. http://www.ukbiobank.ac.uk/assessment/takepart.php
5. http://www.bio-nmd.eu/forPatients/
6. http://society.guardian.co.uk/alderhey/story/0,,450736,00.html
7. http://www.hta.gov.uk/legislationpoliciesandcodesofpractice/legislation/humantissueact.cfm
8. http://jme.bmj.com/content/29/1/4.full
9. http://bulletin.sciencebusiness.net/ebulletins/showissue.php3?page=/548/art/18712/

To comment on this article, visit www.bio-nmd.eu
or email: catherine.turner@newcastle.ac.uk

BIO-NMD is a Translational Research Project – What does this mean?

Translational research bridges the gap between laboratory and patient

Scientists are constantly discovering more and more about the human body. We now understand more than ever the processes which keep us alive and well along with some of the things that go wrong causing disease or ill-health. Much of new discovery and technology comes from basic research which takes place in the laboratories of academic institutions or companies around the world. However, harnessing this knowledge and turning new discoveries into useful, marketable treatments of direct benefit to human health is much more difficult. Translational research aims to overcome this problem. It is research which turns new knowledge and understanding gained in the laboratory into meaningful therapies, drugs or preventative measures which are of direct benefit to patients. In short, it bridges the gap between laboratory and patient.

BIO-NMD does this by trying to identify biomarkers which can be measured in patients' blood or urine to tell doctors more about the type of neuromuscular disease they have and the best treatment programme for them. Biomarkers will also speed up the testing of new drugs which may be of direct benefit to patients' health.

News and Events

BIO-NMD Industry Session

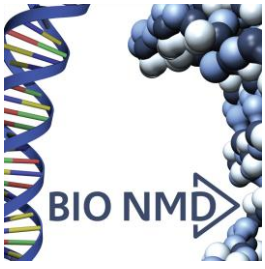
As part of the first project update meeting in July 2010, BIO-NMD hosted an industry session where representatives from a number of different pharmaceutical companies joined in discussions with BIO-NMD partners. Industry involvement will be crucial to the long-term success of the BIO-NMD research – to translate findings into real benefits for patients.

Industry involvement will be crucial to success

Some of the feedback received from participants:

"It was an honour to meet members of the BIO-NMD Team, and I was impressed with their collaborative goal to search for new biomarkers in NMD, bringing them closer to their ultimate aim of "Personalised Medicine" - right drug for the right patient. The industry session was an excellent example of a forward thinking approach in bringing academia and industry closer together, and we would certainly like to be engaged in future meetings"

"Identifying and understanding the mechanisms involved in debilitating diseases like Duchenne Muscular Dystrophy requires an integrated approach of multiple disciplines of both basic and clinical sciences. Translating these mechanisms into medicines also requires knowledge of the biological fingerprint of the disease. Encouragingly the BIO-NMD project has arrived to do exactly that, to help identify and apply such biomarkers to aid diagnosis, track disease progression and to ultimately help establish new treatment options. With multiple partners around the world, the world's best scientists and physicians in this field are now collectively working together with a united vision; to increase the understanding of DMD to implement timely improved treatment options to its sufferers. The BIO-NMD project journey has begun and will be followed with great interest by the pharmaceutical industry and its key stakeholders - the boys and their families. We all look forward to seeing the developments of this exciting and vitally important initiative over the forthcoming years."



Cure CMD and SAM have awarded a $50,000 grant

Dr Jim Collins

Dr. Jim Collins, MD, PhD (james.collins@cchmc.org) at Cincinnati Children's Hospital Medical Center in Cincinnati Ohio, was awarded a $50,000 one year grant from Cure CMD and Struggle Against Muscular Dystrophy (SAM) to investigate the genes and proteins made by genes in people with merosin-deficient congenital muscular dystrophy (CMD). The goal is to identify unique protein and genetic biomarkers which can be used to show disease progression or severity. Blood and urine samples from 14 CMD children are being studied along with controls from unaffected children of the same age and gender.

Merosin-deficient CMD is clinically well defined and the genetic cause has been confirmed – it can be identified by genes and proteins which only occur in patients with the disease. The first results from this study will be used in further studies that we hope will lead to better understanding of how merosin-deficient CMD affects the body and to the discovery of a unique biomarker that could be used in future clinical trials.

Ensuring a standard approach

The Children's National Medical Center and other US sites are working together with TREAT-NMD to ensure that standard procedures for muscle biopsy analysis are followed by centres conducting clinical trials into antisense exon-skipping therapy for patients with Duchenne muscular dystrophy. Called the Biochemical Outcome Measures initiative, the collaboration aims to recommend a standard method for measuring levels of the protein dystrophin in patients undergoing this therapy. An increased level of dystrophin may be an indication that the therapy is effective in that patient. Therefore, an accurate, reproducible and standard method for measuring levels of the protein are expected to be crucial for the success of future trials.

A workshop has been organised for 21st September 2010 at the Institute of Child Health, London. The recommendations and findings of the initiative will be presented and discussed. It is hoped that publication of these recommendations will follow soon after in order that they can be used in future clinical trials.

Please submit news items for future issues to:
catherine.turner@newcastle.ac.uk

Diary dates

Visit the BIO-NMD website for more details of these events

www.bio-nmd.eu/meetings-and-events/scheduled-meetings/

16th – 19th September 2010
EAMDA 40th Annual General Meeting
Milan, Italy

18th September 2010
Muscular Dystrophy Campaign Conference
Hilton Birmingham Metropole, Birmingham, UK

20th – 22nd September 2010
Muscle Study Group Annual General Meeting
Buffalo, New York, USA

21st September 2010
Biochemical Outcome Measures workshop
Initiative partners, researchers and industry
London, UK

12th – 16th October 2010
World Muscle Society International Congress
Kumamoto, Japan

12th – 13th November 2010
Action Duchenne 8th Annual Conference
Hilton Hotel London Canary Wharf, London, UK

1st – 3rd December 2010
BIO-NMD 6 monthly progress meeting
Partners and Patient Association Committee
Montpellier France

Please submit future dates for the Diary to: catherine.turner@newcastle.ac.uk