GUIDELINES FOR LAY REPORT OF THE ENMC WORKSHOPS

- Workshop number
- Title/date/location
- Organizers
- Description of the workshop addressing the following questions :
  (including maximal 250 words per question):

    - What was the background and aim of the workshop (rationale for this workshop, problems to be addressed)?

    - Who attended the workshop (75 words: number of participants, country of origin; patient and/or industry representatives, professional backgrounds)?

    - What was discussed?

    - What were the outcomes and how will they benefit patients? A quote of one of the organizers or participants, a photo of a lively discussion or an important slide that can be disclosed in public, will support the lay report effectively.

    - The following key deliverables were achieved:

        1. …….
        2. …….
        3. …….

    - Road map for the future; what are the future activity plans (e.g. performing future global clinical studies or basic research, sharing data and patients, and/or publishing diagnosis- therapeutic or care guidelines)

    - What are the timelines of these future plan of this consortium and who is taking the lead?

Glossary, suggestions for explanations can be found at http://www.muscular-dystrophy.org/about_muscular_dystrophy/glossary

If required local translations from English can be made by a translation agency in the Netherlands (Elycio Elsevier). For 5 translations (Dutch, German, Italian, French and Danish) this is approximately € 650,00 excluding VAT per workshop (per lay report) and may take 3-4 working days for 5 translations. For one translation the costs are about € 150 and may take 1-2 working days.

It is advisable to appoint a qualified participant (who can be the young researcher from the Young Research Program in collaboration with the patient representative) in preparing notes during the entire workshop to draft the lay report and full paper. Together with the synopses provided by all presenters before the workshop this may assist in a timely submission of the reports to ENMC and the journal of NMD.

The lay report will get an editorial check before publication on the website from the ENMC to fulfil ´lay statement´ requirements.

An example of a lay statement is shown here :

Neuromuscular disorders of mitochondrial fusion and fission – molecular mechanisms and therapeutic strategies

Date: April 26th-28th, 2013
Workshop Number: 197
City: Naarden, The Netherlands

Organisers

Dr. Patrick Yu-Wai-Man (Newcastle, UK); Dr. Valerio Carelli (Bologna, Italia); Prof. Patrick F. Chinnery (Newcastle, UK)

Description

The 197th ENMC workshop entitled "Neuromuscular disorders of mitochondrial fusion and fission – molecular mechanisms and therapeutic strategies" took place from the 26th to the 28thof April 2013 in Naarden, The Netherlands. A multidisciplinary group of 19 participants took part in this workshop, including 18 clinical and basic science researchers from 6 different countries (France, Germany, Italy, Spain, the UK, and the USA), and 1 patient representative from CMT UK.

Background

Mitochondria are essential components of all human cells and they function as very efficient "powerhouses" that produce most of the energy required for normal cell function. If insufficient energy is produced by mitochondria, cells cannot function properly and they eventually die causing a range of human diseases. It is now clear that mitochondria do not exist in isolation, but instead, they form long, branching, tubular networks that extend throughout the cell. Mitochondrial segments break apart and fuse together continuously and this highly dynamic process is tightly coordinated by a number of key proteins. Unsurprisingly, strong evidence has recently emerged implicating disturbed mitochondrial fusion and fission as the explanation for a number of debilitating progressive neuromuscular disorders.
Two major proteins, MFN2 and OPA1, work closely together to coordinate the sequential steps involved in mitochondrial fusion. Mutations in the *MFN2* gene result in autosomal-dominant Charcot-Marie-Tooth disease (CMT-2A). In CMT-2A, the peripheral nerves that supply the arms and the legs get progressively damaged (peripheral neuropathy). As a result, patients develop varying degrees of limb weakness and loss of sensation. Interestingly, *MFN2* mutations have also been found in families with a specific CMT-2A subtype where the peripheral neuropathy is complicated by loss of vision secondary to damage to the optic nerve. The optic nerve is the specialised high-speed cable that sends visual information from the back of the eye to the brain and when damaged, the optic nerve becomes pale (optic atrophy).
Autosomal-dominant optic atrophy (DOA) is an important cause of inherited childhood blindness and it is caused by irreversible optic nerve damage. *OPA1* is the major causative gene and it accounts for about 60% of cases worldwide. Unfortunately, up to 1 in 6 *OPA1* mutation carriers will develop a more severe form of the disease (DOA plus) where visual loss is complicated by the development of prominent neuromuscular features, usually from the third decade of life onwards.

Aim of this workshop

To establish an integrated research network in order to better understand the basic mechanisms responsible for the development of neuromuscular disease in patients harbouring *MFN2* and *OPA1* mutations.

What was achieved?

The first half of this workshop reviewed the fundamental and interrelated roles mediated by the MFN2 and OPA1 proteins in normal cellular function. The pathogenetic mechanisms directly implicated in the development of CMT2A and DOA were discussed in the context of both *in vitro* and *in vivo* disease models. In the second half of this workshop, the participants collectively described the range of clinical features linked to *MFN2* and *OPA1* mutations, including novel disease manifestations and the natural history of this heterogeneous group of disorders. The final session focused on how to translate recent scientific advances for the benefit of patients and the best way to design future clinical trials in this challenging area of research.

The following key deliverables were achieved:

1. A comprehensive description of the expanding neuromuscular phenotypes associated with pathogenic *MFN2* and *OPA1* mutations.
2. Collaborative biobank access to patient tissue samples and animal models to further explore fundamental disease mechanisms in CMT-2A and DOA.
3. Pooled clinical registry of well-characterised patient cohorts for the purpose of future clinical studies, including treatment trials.

Participants

Dominique Bonneau (Angers, France); Karen Butcher (CMT UK Representative); Valerio Carelli (Bologna, Italy); Patrick F Chinnery (Newcastle, UK); Padraig Flannery (Newcastle, UK); Guy Lenaers (Montpellier, France); Deborah Naon (Padova, Italy); Veronique Paquis-Flucklinger (Nice, France); Joanna Poulton (Oxford, UK); Hemachandra Reddy (Portland, Oregon, USA); Mary Reilly (London, UK); Manuel Rojo (Bordeaux, France); Elena Rugarli (Cologne, Germany); Hiromi Sesaki (Baltimore, Maryland, USA); Orian Shirihai (Boston, Massachusetts, USA); Marcela Votruba (Cardiff, UK); Patrick Yu-Wai-Man (Newcastle, UK); Antonio Zorzano (Barcelona, Spain).

A full report of this ENMC workshop will be published in Neuromuscular Disorders.