centers working together is the quick way to do clinical trials and determine the efficacy of new therapies for diseases considered untreated for centuries.

doi:10.1016/j.nmd.2011.06.1026

P4.62
The Jain Foundation: A new paradigm for funding disease research
J.C. Wiley, P. Mittal
Jain Foundation, Bellevue, United States

The Jain Foundation’s mission is to accelerate and develop a therapy for Limb Girdle Muscular Dystrophy 2B/Miyoshi Myopathy, a rare, autosomal recessive muscular dystrophy caused by mutations in the dysferlin gene. We accomplish this through funding, coordinating, and managing global research projects. Since 2005, we have awarded over $7.2 million USD in research support and currently fund 43 research projects in the following areas of study: dysferlin structure/function, ferlin proteins, membrane repair, reactive oxygen species, high-throughput drug screening, gene, protein and cell therapy, calcium and mitochondrial degeneration and other therapeutic strategies. Prior to the establishment of the Jain Foundation, LGMD2B/MM received little attention from researchers due to the lack of funding and resources. To eliminate roadblocks, we developed dysferlin specific resources, cDNAs, antibodies, cell lines, and animal models, and make them available to all researchers. Furthermore, researchers discuss their challenges and share their expertise, protocols, and resources on our online scientific forum, research sharing network, and at our annual dysferlin conference. We also maintain a patient registry with about 700 registrants and facilitate mutational analysis of dysferlin to identify patients for future clinical studies and further our understanding of the disease. Our multi-faceted program and hands on approach to project management establishes a novel paradigm for enabling disease research.

doi:10.1016/j.nmd.2011.06.1027

P4.63
The New Zealand neuromuscular disease registry
M.J. Rodrigues a, R. Roxburgh b, A. Kidd c, R. Patel d, J. Waldron e, G. O’Grady f, D. Love e, G. Hammond-Tooke f, C. Higgins g, H. Rayner h
aMuscular Dystrophy Association of New Zealand, Auckland, New Zealand; bAuckland City Hospital, Neurology, Auckland, New Zealand; cAuckland University Hospital, Neurology, Auckland, New Zealand; dCairns District Health Board, Christchurch, New Zealand; eStarship Children’s Hospital, Paediatric Neurology, Auckland, New Zealand; fAuckland City Hospital, Molecular Genetics Laboratory, Auckland, New Zealand; gOtago District Health Board, Neurology, Dunedin, New Zealand

The Muscular Dystrophy Association of New Zealand has set the establishment of a national registry for neuromuscular disease as one of their main priorities to advance the potential of enabling clinical trials to take place in New Zealand. New Zealand has a relatively small total population just in excess of four million and it is expected that approximately 4000 people have a neuromuscular condition. Standards of care for people with neuromuscular conditions in New Zealand are comparable to much of Europe and North America meaning that selected endpoints used in clinical trials are equally measurable in the NZ population. Most neuromuscular diseases are rare and any study of disease-modifying medication will require the enrolment of participants from many countries to achieve sufficient numbers to draw significant conclusions. Some treatments for neuromuscular conditions are being developed based on the specific genetic cause of the disease and it is therefore important for any registry to also collect genetic information. The New Zealand Neuromuscular Disease Registry working group decided to set up one registry for all neuromuscular conditions, which houses the required separate databases for each condition, rather than individual registries for each condition. The New Zealand Neuromuscular Disease Registry has received ethics approval to collect voluntary participant information. The registry will send anonymised data to international registries approved by the New Zealand Neuromuscular Disease Registry oversight committee including the TREAT NMD databases for Duchenne Muscular Dystrophy and Spinal Muscular Atrophy and the Rochester registry for Myotonic dystrophy. In addition the registry will be a useful resource for locally-based clinicians and researchers thereby increasing the likelihood of obtaining treatments for these diseases in the future.

doi:10.1016/j.nmd.2011.06.1028

P4.64
Monitoring care practices for Duchenne Muscular Dystrophy – the CARE-NMD project
K. Gramsch i, J. Vry j, J. Rahbek k, B. Steffensen b, K. Bushby a, H. Lochmüller l, S. Rodger m, J. Kirschner n
aUniversity Medical Center Freiburg, Neuropediatrics and Muscle Disorders, Freiburg, Germany; bNational Rehabilitation Center for Neuromuscular Diseases, Aarhus, Denmark; cUniversity of Newcastle upon Tyne, Institute of Human Genetic, Newcastle upon Tyne, United Kingdom

Health services research identifies and measures the most effective ways to organize, manage, finance and deliver high-quality care. But for Duchenne Muscular Dystrophy this is very limited and approaches like using mortality rate as care indicator does not give a very detailed insight. In addition a correlation is impossible to make because ICD-10 code covers too many neuromuscular disorders. Also natural history data on DMD with references to steroid use and other treatment recommendations are limited. A different approach is needed. Using Patient registries can be a valuable tool for data collection even so there may be the limit of selection bias. The EU funded 3 year project CARE-NMD (www.care-nmd.eu) will look on the degree of implementation of Care Standards for DMD (Bushby et al., 2010) and the perception of quality of life. For this CARE-NMD will lean onto the health system analysis approach of Donabedian who developed the concept of structure, process and outcome quality for health care systems. Structure quality describes personal, material and organizational resources available to patients. A process indicator may be, e.g. the access and continuity to a specialist or regular physiotherapy and the outcome indicators look at the results of treatment in quality, efficiency and equity in health. Experts outside and inside the project discussed possible DMD care indicators to be used for the CARE-NMD questionnaires. In the CARE-NMD evaluation (online)-questionnaires will be addressed to patients and professionals. The patient’s questionnaire is combined with the questionnaire for professionals around sum-

MYOTONIC DYSTROPHIES: POSTER PRESENTATIONS

P5.1
Overexpression of abnormal DM2 specific splice form, but not endogenous NEDD4 disrupts the turnover of PTEN in muscle
Hyperlipidemia is frequently associated with insulin resistance in Myotonic dystrophy type 2 (DM2) patients, but the treatment of these patients is problematic, due to an increased risk of statin-induced myopathy. In our neuromuscular centre, we have noted a 10-fold increase in susceptibility of DM2 patients to statin induced myopathy. We have examined the frequency of the previously published SIC1B1 risk allele in DM2 patient biopsies and can exclude it as a major cause of increased statin adverse reaction in DM2 patients in Finland. In this study, we compared the global gene expression profiles of muscle biopsies from DM2 patients versus control muscles and expression changes associated with individuals who are on statin medication, with the aim of distinguishing shared affected pathways in a common pathomechanism. The microarray expression profiles were further analysed in multiple DM2 biopsies by RT-PCR, with the aim of identifying aberrantly spliced genes among the abnormally expressed genes. We identified a unique set of dysregulated genes. NEDD4, an ubiquitin ligase, was one of the dysregulated genes in DM2 patient muscles and in individuals with statin-induced changes. Our work demonstrates that NEDD4 is abnormally spliced in DM2, which leads to an aberrant isoform of NEDD4 protein being expressed in DM2 patient muscles. PTEN, a known NEDD4 target, is increased at the protein level and PTEN accumulates in damaged muscle fibres. PTEN is linked to lipid metabolism via phosphoinositide signalling and Statins have been shown to cause a general decrease in the expression of PTEN in normal individuals. We are in the process of over-expressing in cell culture wild-type NEDD4 and DM2 specific splice isoforms and comparing their ability to regulate the turnover of PTEN through ubiquination. Our results suggest that the NEDD4-PTEN ubiquitination pathway becomes dysregulated in DM2 patient’s muscles.

doi:10.1016/j.nmd.2011.06.1030

P5.3
Fatigue and daytime sleepiness scale in myotonic dystrophy type 1
M.C.E. Hermans a, I.S.J. Merkies b, L. Laberge b, E.W. Blom a, E.K. Vanhoutte a, A. Tennant c, C.G. Faber a
a Maastricht University Medical Centre, Neurology, Maastricht, Netherlands; b Spaarne Hospital, Neurology, Hoofddorp, Netherlands; c Université du Québec à Chicoutimi, Département des Sciences de l’éducation et de psychologie, Québec, Canada; d Maastricht University Medical Centre, Clinical Genetics, Maastricht, Netherlands; e University of Leeds, Department of Rehabilitation Medicine, Leeds, United Kingdom

Fatigue and excessive daytime sleepiness are frequent complaints in myotonic dystrophy type 1. These symptoms show overlapping features, making it hard for patients and clinicians to clinically distinguish them. We aimed to construct a combined fatigue and daytime sleepiness rating scale specific for myotonic dystrophy type 1 using the Rasch measurement model. The Rasch Model sets additional quality standards for outcome measures and is widely used for reviewing measurement properties of existing ordinal scales and construction of new scales. Questionnaires, including the Epworth Sleepiness Scale, Fatigue Severity Scale, and Daytime Sleepiness Scale were completed by 354 patients (167 Dutch, 187 Canadian). Data were subjected to Rasch analyses. The initial 22 items did not meet Rasch model expectations. Subsequently, data were tested for required measurement issues such as appropriate response categories, absence of item bias, local response independence, and unidimensionality. After resoring and removing misfitting items, the final 12-item scale showed good model fit and unidimensionality. High internal consistency, discriminative validity and good item difficulty hierarchy were demonstrated. In conclusion, this study addresses various measurement issues required to construct a clinically meaningful scale using Rasch analysis. The final combined fatigue and daytime sleepiness scale (FDSS) specifically developed for myotonic dystrophy type 1 patients provides interval measures on a single continuum. If its responsiveness can be demonstrated, we expect that the FDSS will be valuable for future clinical trials and therapeutic follow-up studies.

doi:10.1016/j.nmd.2011.06.1032

P5.4
Photovoice: Using an innovative qualitative research method to capture the experiences of individuals with myotonic dystrophy (DM1)
K.A. LaDonna, S.L. Venance
University of Western Ontario, London, Canada

Myotonic Dystrophy (DM1) is a multi-systemic disorder that can present with apathy and cognitive impairment. Currently, the experiences of individuals with DM1 are under-represented in the literature, presenting opportunities to explore this population qualitatively. Qualitative methods are gaining acceptance in the medical literature as important tools for studying patient populations. However, given the psychiatric