We are very grateful to Myotubular Trust for supporting our project entitled “High throughput gene sequencing to identify new genes that cause myotubular and Centronuclear Myopathies”. While this project is still ongoing in our laboratory, we have validated our strategy in two recent studies described below:

Next generation sequencing for molecular diagnosis of neuromuscular diseases
Inherited neuromuscular disorders are chronic genetic diseases posing a significant burden on patients and their family. Despite tremendous research and clinical efforts, the molecular causes remain unknown for nearly half of the patients, due to the large number of implicated genes and conventional molecular diagnosis based on a gene-by-gene approach. Our team validated the novel high-throughput sequencing technology to read at once all the 267 genes implicated in different neuromuscular disorders in a group of patients (the “NMDseq” study). We tested our strategy on DNA of patients with known mutations, for example in MTM1, BIN1 or DNM2 in patients with myotubular or centronuclear myopathies, and we unambiguously identified all mutations in a blind assay. Using this novel approach, we also identified mutations in patients awaiting genetic diagnosis, some of whom since more than a decade. In conclusion, this rapid and cost effective approach is suitable for routine genetic diagnosis, and accelerates genetic counseling and access to more specific disease management.

Published in : Vasli et al., Acta Neuropathol. 2012 Aug;124(2):273-83 (http://www.ncbi.nlm.nih.gov/pubmed/22526018)

Identification of the causative gene in the “Samaritan myopathy”, sharing common features with centronuclear myopathies
We were intrigued by a rare myopathy called the “benign Samaritan congenital myopathy” that is characterized by an “inverse” course of disease with patients severely affected at birth, progressively improving and minimally affected at adult stage. Histology partially reveals features of centronuclear myopathy. Using the novel high-throughput technology we have analyzed all the 18,000 genes encoded in the DNA molecule of two patients with this myopathy and identified a novel mutation in the ryanodine receptor RYR1, a molecule important for the regulation of muscle contraction. The identification of the genetic cause in this “inverse” congenital myopathy is the first achievement to further understand how these patients strongly improve and envisaged how a similar improvement can be obtained in patients with other congenital myopathies as myotubular and centronuclear myopathies.

Published in : Böhm et al., Acta Neuropathol. 2012 Oct;124(4):575-81 (*http://www.ncbi.nlm.nih.gov/pubmed/22752422*)

Dr Jocelyn Laporte, Strasbourg, France
May 2013