Application of disease maps to rare diseases: neuromuscular diseases

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Neuromuscular diseases are a heterogeneous group of neurological conditions. Most of them are inherited, with over 400 genes identified, and rare due to their very low individual prevalence. However, as a whole they are as prevalent as common neurological conditions such as Parkinson´s disease and multiple sclerosis. Based on the anatomical origin of the primary defect they are classified as motor neuron diseases (including spinal muscular atrophy and amyotrophic lateral sclerosis), peripheral neuropathies, myasthenic syndromes (neuromuscular junction) and myopathies and dystrophies (muscle fibre). Although each of them is characterized by a set of clinical and pathological hallmarks, they share some common mechanisms such as fibrosis, inflammation, mitochondrial dysfunction, muscle fibre degeneration and impaired regeneration.

In the last few years we have seen a significant development of clinical trials based on molecular therapies or pharmacological modulation of downstream pathways. At present there are two FDA-approved drugs for spinal muscular atrophy and Duchenne muscular dystrophy (DMD). However, a limitation for research and further therapy development in neuromuscular diseases is the fractionation of knowledge and the limited integration between studies, even at the high-throughput data level.

Duchenne muscular dystrophy is the most common form of the childhood muscular dystrophies and a paradigm for degenerating muscle diseases. It is caused by mutations in the DMD gene leading to the deficiency of the dystrophin protein from the sarcolemma of muscle fibres. The aim of this project is to generate a repository that describes molecular mechanisms of DMD (the "DMD-map"), and that supports biomarker identification, omics data interpretation, identification of disease types, mapping drug action mechanisms, developing predictive models and suggesting therapeutic strategies. The DMD-map will be the first stage for building a disease map of myopathies (MyoMap) using the information and experience gained in constructing the DMD-map.