Neuromuscular Research

Translational Research in Neuromuscular Diseases

Our Neuromuscular Research Laboratory, Clinic of Neurology and Department of Biomedicine, focuses on the elucidation of pathophysiological mechanisms involved in neuromuscular diseases and on the development of therapeutic strategies. Myotonic dystrophy type I (DM1) is a disabling neuromuscular disease with no causal treatment available. It is the most prevalent muscular dystrophy in adults, affecting about 1 in 10'000 individuals. This disease is caused by expanded CTG trinucleotide repeats in the 3’ UTR of the dystrophia myotonica-protein kinase gene (DMPK). On the RNA levels, expanded (CUG)n repeats form hairpin structures that sequester splicing-factors, such as muscleblind-like 1 (MBNL1). Lack of available MBNL1 leads to mis-regulated alternative splicing of many target pre-mRNAs, causing multisystemic involvement in DM1.

In a broader context we are interested in the disruption of the proteostasis network as a possible pathomechanism for diseases affecting skeletal muscle. In collaboration with the research group of Prof. Markus Rüegg, Biozentrum Basel, we are investigating the implications of mTOR deregulation on muscle homeostasis and are studying the function and regulation of atrogenes, in particular the regulation of P62 and FOXO3. This allows us to test novel therapeutic approaches. A prerequisite for successful animal studies using genetic mouse models is an accurate genotyping protocol. Unfortunately, the lack of robustness of the currently available genotyping protocols for the Dysf tm1Kcam mouse strain Dysf tm1Kcam. This genetic characterization enabled us to establish a reliable method for genotyping of the Dysf tm1Kcam mouse model, and thus has made efficient colony management possible. These results will help the scientific community to use the Dysf tm1Kcam mouse model for future studies on dysferlinopathies.

In collaboration with our colleagues from pathology, genetics, plastic surgery, pulmonary medicine, rehabilitation, ergo-, physio- and speech therapy as well as social services, we provide clinical and electrophysiological evaluation, perform muscle and nerve biopsies with histopathological and biochemical workup, genetic workup and counseling, rehabilitation, ergo-/physio- and speech therapy as well as assistance in social matters. Novel clinical observations are being worked up scientifically and from the basis for translational research projects.

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Selected Publications
