

Proteostasis regulators in neuromuscular diseases – learning from zebrafish models

Abstract

Protein homeostasis or proteostasis is crucial for the neuromuscular system and several mutations in proteostasis-related genes are causally linked to neuromuscular diseases. Proteostasis is controlled by various cellular factors that regulate initial protein biosynthesis and folding but also the quality control and degradation of proteins by the proteasome and/or by autophagy. Several zebrafish models of neuromuscular diseases related to proteostasis regulating genes have been generated over the past decades. Zebrafish are vertebrates with similar composition and structure of the neuromuscular system as humans. Furthermore, zebrafish can easily be genetically modified and due to their optic transparency, cells can be directly imaged in live intact animals. Here we will present an overview over existing zebrafish models and we will present our own preliminary data on recently generated and analyzed zebrafish mutants of *valosin-containing protein (vcp)* and PI(3,5)bisphosphate regulators. Using *in vivo* timelapse imaging and ablation experiments we study their biology during development and/or regeneration and compare the results with human biopsy material. The results derived from these models shed light into the pathophysiology of related neuromuscular diseases and can guide therapeutic considerations.