Myofibrillar myopathies (MFM) are progressive diseases of human heart and skeletal muscle with a severe impact on the quality of life and life expectancy of affected patients. They are histopathologically characterized by desmin-positive protein aggregates and myofibrillar degeneration. Although during the last decade some MFM disease genes, encoding sarcomeric and extra-sarcomeric proteins such as desmin, filamin C, plectin, VCP, ZASP, myotilin and αB-crystallin, could be identified, most genetic causes are still unknown due to the lack of families suitable for classical linkage analyses. Furthermore, the precise mechanisms and signaling events that translate MFM-causing mutations into the myopathic phenotype are not well understood even though they are of immense clinical importance for the development of specific therapies.
Selected Publications:


During the last decade, we successfully used forward and reverse genetic strategies in the zebrafish model to dissect novel molecular causes and mechanisms of heart and skeletal muscle myopathies. In an attempt to develop novel targeted treatment strategies for human MFM diseases, our research aims to elucidate further the genetic basis and the precise molecular mechanisms that translate known MFM mutations into the myopathic phenotype by using forward and reverse genetic approaches in zebrafish.

**Nexilin** is expressed in the heart (A, B) and skeletal muscle (A) during zebrafish development. Loss of Nexilin function leads to severe cardiac and skeletal muscle myopathy. Transmission electron microscopy analysis of skeletal muscle (skm) ultrastructure from stimulated Nexilin-deficient (MO-nexilin) (D) and Control (MO-ctrl) (C) zebrafish embryos. Sarcomeric Z-disks appear irregular and detached in Nexilin-deficient embryos.

During the last decade, we successfully used forward and reverse genetic strategies in the zebrafish model to dissect novel molecular causes and pathways involved in the pathogenesis of myopathies, genetic animal models, such as the zebrafish (Danio rerio), have proven extremely helpful. One of the most important advantages of the zebrafish model is the fast development and transparency of the zebrafish embryo that allows easy and direct in vivo analysis of heart and skeletal muscle development, structure and function using light microscopy. Most important is the fact that zebrafish embryos with cardiac dysfunction are still able to develop to early larval stages since the lack of blood circulation can be compensated by absorbing oxygen through the skin.