The role of Dystrophin in muscle maintenance within the zebrafish embryo and the identification of zebrafish models of human muscular dystrophy

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Large-scale mutatgenic screens of the zebrafish genome have identified numerous mutations that disrupt differentiation and maintenance of skeletal muscle within the zebrafish embryo. Mutants possess phenotypes that range from a failure of myoblasts to elongate and fuse into a mulinucleate muscle fibres to those that exhibit muscle degeneration reminiscent of human muscular dystrophies. Homozygous mutants of this latter class form myofibrils normally but are lost focally or globally, depending on the loci involved, during early larval life. Here we present data specifically on one member of the zebrafish dystrophic mutant class and reveal that its phenotype results from mutations within the zebrafish Dystrophin orthologue. We will present a detailed characterisation of the phenotype that arises as a consequence of the loss of Dystrophin expression within the embryonic and larval myotomes of zebrafish. This analysis points to the critical and novels roles that the Dystrophin and its associated-glycoprotein complex plays in the ontogeny of zebrafish muscle. We will compare and contrast the function of Dystrophin in teleost and mammalian muscle fibre biogenesis. This analysis represents the first identification of a zebrafish model of a human muscular dystrophy and we will discuss the possible application of zebrafish genetic methodologies to the study of the human dystrophic condition.