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Minireview

Muscle growth patterns and regulation during fish ontogeny

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Abstract

In fish, the skeletal muscle of the trunk and the tail derives from the somites which form in the paraxial mesoderm in a rostro-caudal sequence. The development of the fish myotome begins with the onset of myogenic regulatory factors expression and continues with the formation of a distinct superficial layer of slow muscle fibres that covers a bulk of fast muscle fibres located in the deep portion of the myotome. Muscle fibres of the slow-twitch lineage originate in fish embryos from adaxial cells, a distinct subpopulation of the paraxial mesoderm that flanks the notochord. During the early maturation of the somite these adaxial cells migrate away from the notochord towards the lateral part of the somite where they form the superficial slow fibres. Lateral presomitic cells that remain deep in the myotome differentiate into fast muscle fibres. Morphogens of the hedgehog family secreted by the notochord have a pivotal role in inducing the slow-twitch lineage. In late embryos, additional fibres are added from discrete germinal zones situated at the ventral and dorsal extremes of the developing myotome. This regionalised process has been termed "stratified hyperplasia." In fish which grow to a large final size this is followed by a mosaic hyperplastic process that leads to the formation of new fibres throughout the whole myotome. Current knowledge about the endocrine and autocrine factors that potentially regulate the proliferation and the differentiation of muscle cells within the embryonic and larval fish myotome is reviewed.

Keywords: Teleost; Muscle differentiation; Muscle growth; Endocrine factors; Autocrine factors; Myostatin; IGFs; FGFs

1. Development of the myotome

1.1. Somitic muscle precursors formation

In fish, as in other vertebrates, skeletal muscle derives from the somites that are formed during the rostro-caudal segmentation of the paraxial mesoderm. Recent data suggest that a segmentation clock controlling cyclic Notch signalling is involved in concert with fgf/MAPK signalling, in the periodic formation of somite boundaries (Saga and Takeda, 2001). After the segmentation, in interaction with surrounding tissues, the somite is patterned into different compartments. The ventral somitic domain gives rise to cells of the sclerotome. These cells that express *pax 9* (Nornes et al., 1996), *twist* (Stickney et al., 2000), and collagen I (Rescan et al., 2005) will form the axial skeleton (Morin-Kensicki and Eisen, 1997). A large portion of the somite situated above the sclerotomal cells contributes to the formation of muscle precursor cells (Currie and Ingham, 1998).

1.2. Expression of myogenic regulatory factors in developing myotome

The specification of muscle precursor cells in fish embryos begins before the onset of somitogenesis with the expression of MyoD and Myf5 in the paraxial mesoderm (Rescan, 2001). MyoD and Myf5 together with myogenin and mrf4 are myogenic regulatory factors (MRF) sharing a conserved central region termed the basic/helix–loop–helix (bHLH) domain. The basic domain mediates sequence-specific DNA binding, whereas the helix–loop–

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helix domain regulates dimerisation with the universal proteins E12 or E47, which are encoded by the E2A gene. The heterodimer thus formed binds to E box, a DNA motif present in promoters of skeletal muscle-specific genes. Such a binding is involved in the transcriptional activation of the E-box containing gene. While initial expression of MyoD in zebrafish is restricted to the medial (adaxial) cells of the paraxial mesoderm close to the notochord (Weinberg et al., 1996), myf5 expression takes place in both adaxial and lateral cells of the paraxial mesoderm (Chen et al., 2001) suggesting different roles for these two MRFs in regulating early myogenesis. Two MyoD orthologs co-exist in trout genome, but only one (TMyoD) is expressed in medial cells of the presomitic mesoderm (Fig. 1A); the other MyoD ortholog (TMyoD2) is activated only in the posterior compartment of the neoformed somite (Delalande and Rescan, 1999). Interestingly, the composite expression pattern of TMyoD and TMyoD2 in trout embryos is reminiscent of the expression pattern of the single MyoD gene in zebrafish. This suggests, according to the duplication–degeneration–complementation model developed by Force et al. (1999), that the two trout Myod orthologs have evolved in such a way that they complement each other to fulfil the function of the single MyoD gene present in the zebrafish genome. Myogenin expression patterns are similar in zebrafish and trout embryos: in both fish species, myogenin expression first occurs in MyoD-expressing medial cells of the forming somite; during somite maturation, myogenin expression extends from the medial to lateral regions of the somite. Orthologs of mrf4 have also been identified in a few fish species including the zebrafish and *Tetraodon nigroviridis*. However, the expression pattern of mrf4 in fish embryos has not yet been reported. The expression of muscle-specific genes in developing fish myotome clearly follows that of the myogenic regulatory factors (Rescan et al., 2001a; Xu et al., 2000).

1.3. Slow and fast muscle type differentiation

In most fish, slow and fast muscle fibres occupy distinct regions of the axial muscle. A superficial layer of slow oxidative fibres (red muscle) covers a deeper, larger mass of fast glycolytic fibres (white muscle). Intermediate muscle fibres (pink muscle) frequently are located between the slow and fast muscle fibres. Our understanding of fish muscle formation has been expanded by the findings of Devoto et al. (1996) showing that the slow fibres originate from a group of medial (adaxial) cells initially present in the paraxial mesoderm. These adaxial cells that form an epithelial-like monolayer flanking the notochord are the first to express MyoD. Using dye tracing Devoto et al. (1996) have shown that injected adaxial cells migrate radially away from the notochord to form a superficial, subcutaneous layer of muscle cells at the lateral-most-extent of the myotome. In agreement with this morphogenetic pattern, immunolocalisation of slow myosin in zebrafish (Blagden et al., 1997; Devoto et al., 1996) and in situ hybridisation of slow MyLC and MyHC mRNAs in trout (Chauvigné et al., unpublished data; Rescan et al., 2001a) reveal an apparent migration of adaxial cells toward the outermost part of the myotome. In zebrafish, a subset of adaxial cells (called the pioneer cells) that expresses the engrailed antigens

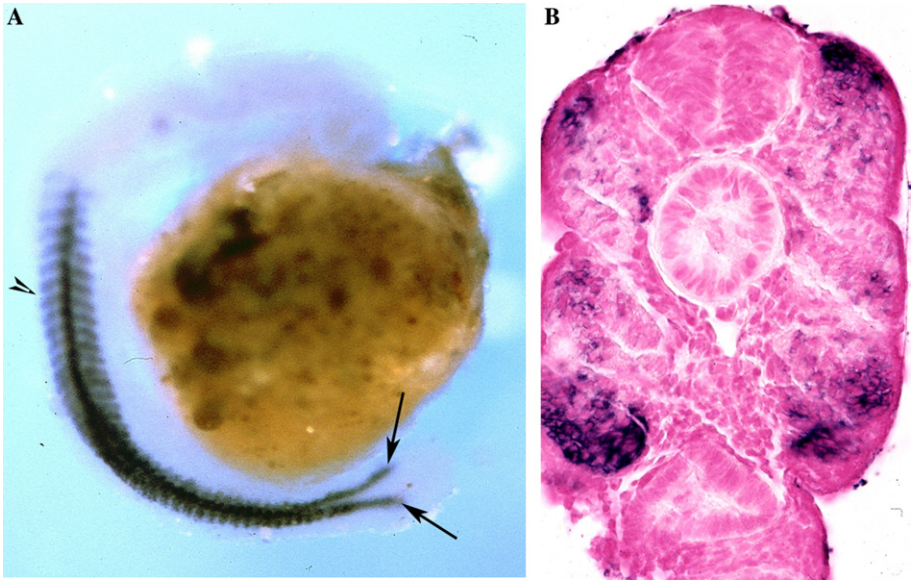

Fig. 1. (A) Expression of TMyoD in a 45-somite trout embryo. Rostrally TMyoD transcript is visualised in most part of the somite (arrowhead) while in the caudal paraxial mesoderm, TMyoD transcript is restrictedly present in two rows of medial cells adjacent to the axial structures (arrows). (B) Expression of myogenin in a late eyed trout embryo. Myogenin transcript is present in dorsal and ventral domains of the myotome indicating that new fibres differentiate at their levels.