DEVELOPMENTAL DYNAMICS 236:2432–2443, 2007

SPECIAL ISSUE REVIEWS–A PEER REVIEWED FORUM

The Teleost Dermomyotome

Frank Stellabotte and Stephen H. Devoto*

Recent work in teleosts has renewed interest in the dermomyotome, which was initially characterized in the late 19th century. We review the evidence for the teleost dermomyotome, comparing it to the more well-characterized amniote dermomyotome. We discuss primary myotome morphogenesis, the relationship between the primary myotome and the dermomyotome, the differentiation of axial muscle, appendicular muscle, and dermis from the dermomyotome, and the signaling molecules that regulate myotome growth from myogenic precursors within the dermomyotome. The recognition of a dermomyotome in teleosts provides a new perspective on teleost muscle growth, as well as a fruitful approach to understanding the vertebrate dermomyotome. *Developmental Dynamics 236:2432–2443, 2007.* © 2007 Wiley-Liss, Inc.

Key words: myotome; anterior border cells; cell fate; paraxial mesoderm; somite; zebrafish; fast muscle; pax7; myogenesis; ABC

Accepted 5 June 2007

INTRODUCTION

Segmentation of the trunk musculoskeletal system is an obvious and universal characteristic of vertebrates. In adult teleosts, as in most adult aquatic vertebrates, segmentation is most visible in the overt reiteration of the myotomes, which is the axial musculature used for swimming. In contrast, in most adult land vertebrates, including amniotes, segmentation is most visible in the skeletal elements of the axial skeleton, which needs to be more robust to support a body out of water.

Segmentation begins in the early embryo, when the paraxial mesoderm becomes subdivided into metameric units called somites. Shortly after segmentation, three distinct tissues can be distinguished within the somite (Fig. 1, Kaestner, 1892): the sclerotome forms the axial skeleton, the myotome forms the axial musculature, and the dermomyotome forms the axial dermis and generates precursors for myotome growth (Box 1). Somites initially form as columnar epithelial cells surrounding a mesenchymal core. The dermomyotome becomes distinct in the dorsal and/or lateral aspect of the somite, as the sclerotome precursors become mesenchymal, and the early myotome cells begin to differentiate into muscle fibers.

The teleost dermomyotome was initially identified, in the 19th century, in the same manner as was the amniote dermomyotome—by developmental stage of origin, position, morphology, and the speculated fates of its cells. As in amniotes, the teleost dermomyotome can be identified shortly after somite formation as an epithelial layer of proliferative cells on

Box 1 The tissue that we now call the dermomyotome has had many names since its first description. Most of these names have been inspired by its position in the somite, and been relatively neutral about its cellular fate(s) (for a review of the early nomenclature, see Gadow and Abbot, 1895). In German, it was "peripherer Theil des Urwirbel" (peripheral part of the segment/somite, e.g., Ehrlich, 1875), "Coriumblatt" (dermal sheet, e.g., Kaestner, 1892), or "Cutisblatt" (skin sheet, e.g., Maurer, 1894); in French, "Fuillet Externale" (external layer, e.g., Sunier, 1911); in English, "Dermatome" (dermal section, e.g., Lillie, 1919) or "External Cells" (Waterman, 1969). Although some early writers used the term dermomyotome in the same manner as we do now (e.g., Williams, 1910), the term did not gain widespread use until after lineage labeling experiments confirmed that this layer was not just an aggregation of separate dermis and muscle precursors, but rather a precursor to both dermatome and myotome.

Department of Biology, Wesleyan University, Middletown, Connecticut
Grant sponsor: NIH; Grant number: R01 HD37509; Grant number: R01 HD044929.
***Correspondence to: Stephen H. Devoto, Department of Biology, Wesleyan University, Middletown, CT 06459. E-mail: sdevoto@wesleyan.edu**

DOI 10.1002/dvdy.21253
Published online 24 July 2007 in Wiley InterScience (www.interscience.wiley.com).

the external surface of the embryonic myotome (Waterman, 1969; Veggetti et al., 1990; Johnston, 1993; Ramirez-Zarzosa et al., 1995; Lopez-Albors et al., 1998; Stoiber et al., 1998; Dal Pai et al., 2000; Steinbacher et al., 2006, 2007). In many species, specialized junctions connect adjacent cells within the dermomyotome. As in amniotes, the teleost dermomyotome gives rise to muscle fibers (Kaestner, 1892; Hollway et al., 2007; Stellabotte et al., 2007). More recently, the teleost dermomyotome has been shown to express the same genes expressed in the amniote dermomyotome, including *pax3*, *pax7*, *dacD*, and *meox* (Groves et al., 2005; Devoto et al., 2006; Feng et al., 2006; Hammond et al., 2007; Hollway et al., 2007).

Although the dermomyotome in all teleosts consists of an undifferentiated layer of epithelial cells external to the myotome, the thickness of the dermomyotome can vary dramatically between different teleosts. For example, the dermomyotome of trout and cichlid is a thick, robust epithelium with well-developed dorsal and ventral lips similar to those in amniotes (Devoto et al., 2006; Steinbacher et al., 2007). In contrast, the dermomyotome of zebrafish and tuna is a flattened epithelium with no obvious dorsal and ventral lips (Devoto et al., 2006). The variation in the thickness of the dermomyotome does not correlate with phylogenetic relationships or ultimate body size. Similar variation exists within tetrapods: the dermomyotome in *Xenopus* is a flattened epithelium much more similar to that of zebrafish than that of amniote tetrapods (Grimaldi et al., 2004).

Recent work in the chick and the mouse has dramatically expanded our understanding of the dermomyotome in these two model amniotes. The dermomyotome is now known to consist of proliferative, multipotent precursors to many different cell types. In addition to axial muscle, the dermomyotome gives rise to dermis, appendicular muscle, and angiogenic cells of the trunk and limb vascular and lymphatic vessels (for review, see Brand-Saberi and Christ, 2000). The dermomyotome epithelium thins and eventually disappears as its cells enter the myotome or dermis, or differentiate into other cell types. The last regions of the dermomyotome to disappear in amniotes are the dorsomedial and ventrolateral lips.

The dermomyotome has been identified in all vertebrates that have been examined, including agnathans, chondrichthyans, anamniote tetrapods, chondrostean actinopterygians, and teleosts (reviewed in Kusakabe and Kuratani, 2005; Devoto et al., 2006). Changes in dermomyotome patterning may underlie evolutionary changes in vertebrate body plans. However, very little is known about the development and differentiation of the dermomyotome in species other than chick and mouse. For many years, muscle growth has been extensively studied in teleost species used in aquaculture. More recently, the zebrafish has emerged as a powerful teleost model system in which to apply genetic and cellular techniques for understanding vertebrate development. The use of teleosts to study the dermomyotome promises to not only address long-standing questions about dermomyotome development that have proven difficult to answer in amniotes, but also provide insights into the similarities and differences between the amniote and teleost dermomyotome.

We present here a review of the dermomyotome in teleosts, focusing on recent discoveries using the analysis of gene expression, lineage tracing, and genetics. We highlight similarities and differences between the teleost and the better-studied amniote dermomyotome. We discuss the formation of the embryonic myotome, the formation of the dermomyotome, the differentiation of the dermomyotome into axial muscle and dermis, the signaling molecules that regulate dermomyotome differentiation into muscle fibers, and the cellular rearrangements occurring during dermomyotome development. Finally, we highlight important questions that remain about the teleost dermomyotome.

PRIMARY MYOTOME FORMATION

The teleost dermomyotome becomes distinct only after the formation of a primary myotome. The primary myotome forms quite early in most teleosts and consists of a superficial layer of slow muscle fibers over a deeper mass of fast muscle fibers (Fig. 2D,E; Stickney et al., 2000; Scaal and Wiegreffe, 2006). The first of these muscle fibers to differentiate are the slow muscle fibers, which develop from cells adjacent to the axial mesoderm (the notochord). These slow muscle precursors, also called adaxial cells, are the most medial paraxial mesoderm cells and have been identified by morphology or by gene expression in all teleosts that have been examined, including zebrafish (Thisse et al., 1993), herring (Temple et al., 2001), trout (Delalande and Rescan, 1999), pearlfish (Steinbacher et al., 2006), flounder (Zhang et al., 2006), and carp (Cole et al., 2004). Adaxial cells begin to differentiate while still in the segmental plate—proteins of the contractile apparatus such as myosin and tropomyosin are expressed very early in most teleosts that have been investigated. In trout and zebrafish, adaxial cells initially express properties of both slow and fast muscle fibers (Xu et al., 2000; Rescan et al., 2001). Shortly after their incorporation into somites, these differentiating slow muscle fibers elongate, and myofibrils appear (O'Connell, 1981; Stoiber et al., 1998; Dal Pai-Silva et al., 2003). Once slow fibers are fully elongated, they are functional cells each with a single, relatively large nucleus, forming a monolayer on the external surface of the embryonic myotome, underneath the dermomyotome (discussed below). The deep, fast muscle fibers form the second component of the primary myotome. Shortly after segmentation, as the slow fibers on the medial surface of the somite begin to differentiate, cells in the posterior of the somite begin to express myogenic regulatory factors (MRFs; Weinberg et al., 1996; Delalande and Rescan, 1999; Temple et al., 2001; Cole et al., 2004; Steinbacher et al., 2006; Zhang et al., 2006). These posterior somite cells then elongate and differentiate into medial fast muscle fibers (Fig. 2A–C; Stellabotte et al., 2007).

Several lines of evidence suggest that the primary myotome develops independently of the dermomyotome. First, both the adaxial cells and the

posterior somite cells are postmitotic before their incorporation into a somite (Barresi et al., 2001; Stellabotte et al., 2007). Second, they express MRF genes very early, before or during the time that they become incorporated into a segment (Weinberg

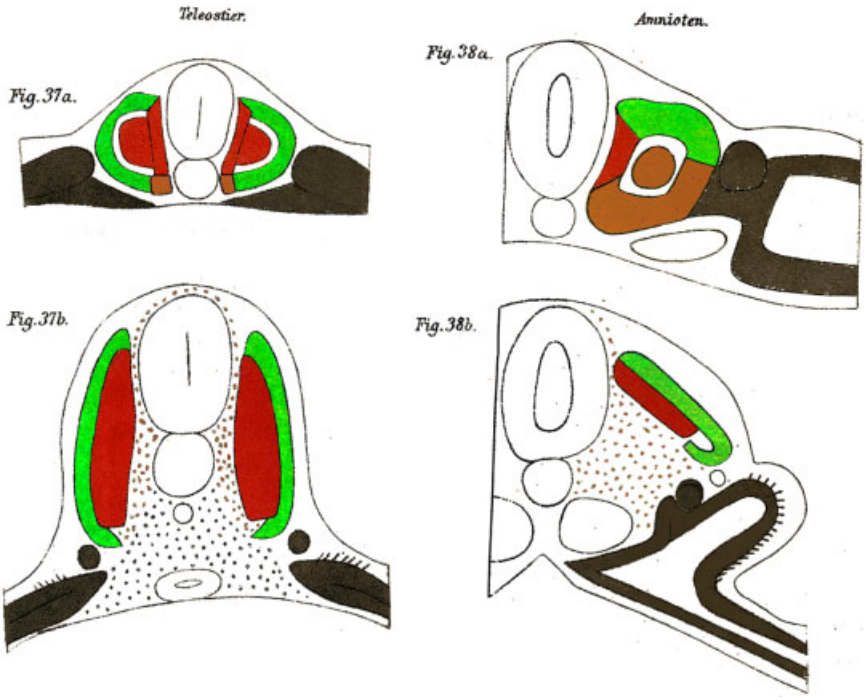

Fig. 1. Teleost and amniote embryos share somitic compartments. Schematic representations of transverse views of teleosts embryos (left) and amniote embryos (right). In nascent teleost somites (top left), medial cells (red) begin elongating into the primary myotome, while dermomyotome cells (green) are found laterally. Sclerotome cells (brown) initially occupy ventromedial locations within the somite. As the teleost somite matures (bottom left), dermomyotome cells remain on the external surface, the myotome expands from medial to lateral, and sclerotome cells migrate dorsally to surround the notochord and neural tube. In an epithelial amniote somite (top right), the dermomyotome forms from the dorsal aspect (green) of the somite as the ventromedial cells (brown) give rise to sclerotome. The first cells to elongate into the primary myotome are in a dorsomedial location (red). As the amniote somite matures (bottom right), dermomyotome cells are found external to the myotome and sclerotome cells migrate dorsally to surround the notochord and neural tube. Modified from Kaestner (1892).

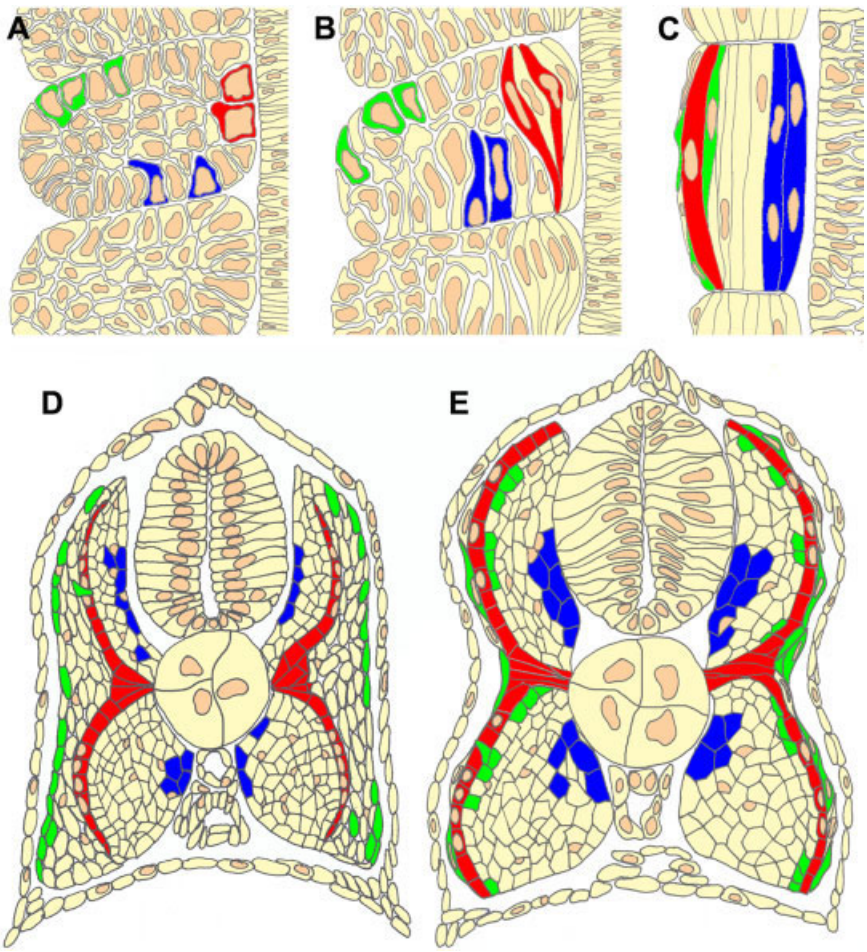

Fig. 2. Dermomyotome and myotome morphogenesis. A–C: A schematic time series of dorsal views of somites (modeled after zebrafish); anterior is up and the midline is to the right. **A:** In nascent somites, epithelial border cells surround a mesenchymal core. The anterior border cells (ABCs) are the anterior-most row of cells lateral to the adaxial cells which line the notochord. **B:** The fate of subsets of ABCs (green), posterior cells (blue), and adaxial cells (red) are shown once the somite loses its epithelial morphology. Adaxial cells elongate into slow muscle fibers (red) along the notochord, as posterior cells initiate elongation (blue), and ABCs (green) move laterally. **C:** At 24 hr, the posterior cells (blue) have elongated into medial fast fibers and a subset of the dermomyotome cells (green) have elongated medial to the superficial slow muscle layer (red). Some of the dermomyotome cells remain external to the myotome as a layer of flattened cells (green). **D,E:** Schematics depicting transverse sections through the midtrunk somites of an embryo partly through the segmentation period (20 hr in zebrafish, D) and at the end of the segmentation period (24 hr in zebrafish, E). Adaxial cells give rise to superficial slow fibers (red). ABCs give rise to dermomyotome cells on the external surface of the somite (green) at mid-segmentation stages and then to dermomyotome as well as lateral fast fibers by the end of the segmentation stage (green). Posterior cells (blue) have already elongated into muscle fibers at the 20-hr stage (D) and occupy distinct, medial positions in the 24 our myotome (E).

et al., 1996; Delalande and Rescan, 1999; Temple et al., 2001; Cole et al., 2004; Steinbacher et al., 2006; Zhang et al., 2006). Third, they generate early myotome cells exclusively (Hollway et al., 2007; Stellabotte et al., 2007). Finally, adaxial cells and posterior somite cells never express detectable levels of the dermomyotome markers *pax7*, *meox*, or *dacD* (Groves et al., 2005; Hammond et al., 2007; Hollway et al., 2007).

The primary myotome in chick and mouse shares several features with that in teleosts. In both of these amniotes, the earliest myotome consists of mononucleated, slow myosin-expressing cells with relatively large nuclei (Kahane et al., 1998; Kahane and Kalcheim, 1998; Venters et al., 1999). These slow muscle fibers form a monolayer on the external surface of the embryonic myotome, deep to the dermomyotome. However, there are two conflicting groups of models to explain the development of the amniote primary myotome. The first group of models proposes that the cells of the primary myotome originate in the medial edge of the dermomyotome called the dorsomedial lip (DML) (Kaehn et al., 1988; Denetclaw et al., 1997; Williams and Ordahl, 1997; Gros et al., 2004), in other words, the primary myotome in these models does not develop before and independent of the dermomyotome. The second group of models proposes that cells within the dorsomedial half of epithelial somites are postmitotic and migrate rostrally to generate the first elongated myotome cells (Kahane et al., 1998, 2007). These cells, called avian muscle pioneers, arise before dissociation of the somite. MRF gene expression begins in epithelial somites, before the establishment of a molecularly or morphologically identifiable dermomyotome in mouse (Ott et al., 1991), and in quail (Pownall and Emerson, 1992; Borycki et al., 1998), in support of a dermomyotome-independent origin for the primary myotome in these species. In *Xenopus* as well, MRF genes are expressed before the establishment of a dermomyotome most abundantly in medial cells of the paraxial mesoderm and, after segmentation, the somite (Hopwood et al., 1991, 1992). In sum, in both tetrapods and teleosts, the expression of the first muscle-specific genes occurs before the establishment of the dermomyotome. A major difference is that in amniotes the first fibers elongate after the dermomyotome has formed, whereas in teleosts and amphibians, the first fibers elongate long before the dermomyotome forms.

DERMOMYOTOME FORMATION

The initial clue to the cellular origin of the dermomyotome in teleosts came from the observation that the medial and posterior cells of the epithelial somite express MRF genes, while the anterior cells do not, in zebrafish (Weinberg et al., 1996), herring (Temple et al., 2001), trout (Delalande and Rescan, 1999), pearlfish (Steinbacher et al., 2006), and carp (Cole et al., 2004). In many teleosts, the *myoD*-negative cells form a single row of epithelial cells at the anterior border of recently formed somites. We have consequently called these cells anterior border cells (ABCs, Stellabotte et al., 2007), to distinguish them from cells on the posterior and interior of the somite; ABCs have also been called Row 1 cells (Hollway et al., 2007). The lack of MRF expression in ABCs at the time of segmentation suggested that these cells do not immediately differentiate into muscle fibers. As somites mature (after approximately 10 further have formed) and the posterior cells have begun to elongate, dermomyotome-associated genes such as *pax7*, *pax3*, *meox*, and *dacD* are expressed in anterolateral cells of the somite in zebrafish and trout (Groves et al., 2005; Hammond et al., 2007; Hollway et al., 2007; Steinbacher et al., 2007). Following further development, these dermomyotome-associated genes are expressed in cells external to the myotome.

Single-cell lineage tracing and time-lapse microscopy has confirmed that the anterior cells of recently formed somites in zebrafish move along the anterior border of the somite to the lateral surface (Hollway et al., 2007; Stellabotte et al., 2007). When ABCs were examined 4–8 hr after injection with vital dye, almost all had developed into flat dermomyotome cells on the external surface of the superficial slow muscle fibers. At this early time, the only nondermomyotome fate of ABCs was muscle fibers, likely after developing into dermomyotome cells (Stellabotte et al., 2007). During the late segmentation and early larval stages, dermomyotome cells proliferate (Hammond et al., 2007; Hollway et al., 2007), and give rise to secondary myotome, mesenchyme cells of the dorsal fin, fin muscle, and possibly dermis (discussed below, Hollway et al., 2007; Stellabotte et al., 2007), Because nearly all ABCs become dermomyotome cells first, it is likely that all of these cell types are derived from the dermomyotome.

The anterior position of dermomyotome precursors in the newly formed somite in teleosts contrasts with the dorsolateral position of dermomyotome precursors in newly formed somites in mice (Eloy-Trinquet and Nicolas, 2002) and chick (Stern and Canning, 1990; Selleck and Stern, 1991). However, in other tetrapods the anterior cells of the somite may also develop into a dermomyotome. Rearrangements of cells in the somites of *Xenopus* bring cells from the anterior of the somite to the external surface (Afonin et al., 2006), where an epithelial layer of undifferentiated, *pax3*-positive cells forms a dermomyotome (Grimaldi et al., 2004). These movements, which have been termed "somite rotation," suggest that the *Xenopus* dermomyotome also derives from anterior border cells of the somite. However, this type of cellular rearrangement has not been seen in other amphibians (Keller, 2000), and it remains unknown how the dermomyotome forms in these embryos. Variations in the mechanisms of segmentation and dermomyotome formation in closely related amphibian species raise the possibility that dermomyotome formation within different species of teleosts or even within different species of amniotes may also show variation. This variation can be investigated by the characterization of dermomyotome formation in a wider range of vertebrates.

Somite patterning, the process by which the different tissues and cell types within the somite become established, has generally been thought of as occurring solely in the mediolateral and dorsoventral dimension. However, especially in teleosts and am-

phibians, segmentation and dermomyotome formation are a result of molecular and morphological events occurring in the same tissue at the same time during embryogenesis. While the signaling mechanisms that regulate the subdivision of the dermomyotome into myotome and dermis are becoming clearer, at least in amniotes (see below for teleosts), very little is known about the signaling mechanisms that regulate the patterning events that lead to the initial formation of the dermomyotome (Wagner et al., 2000). The formation of the teleost dermomyotome from segmentally repeated ABCs that move to a lateral position in the somite suggests a new dimension to somite patterning. Several transcription factors, signaling molecules, and cell surface proteins show restricted expression in either ABCs or posterior somite cells in zebrafish (Holley, 2007). These provide candidate molecules for the patterning of the somite into posterior primary myotome and anterior dermomyotome precursor cell populations. Many of these are implicated in the segmentation process, further work is needed to test whether any also play a role in somite patterning.

DERMOMYOTOME CONTRIBUTIONS TO MYOTOME GROWTH

In teleosts, the earliest growth of the primary myotome occurs by stratified hyperplasia, in which new muscle fibers are added to localized regions of the myotome called germinal zones (Rowlerson and Veggetti, 2001; Rescan, 2005). New muscle fibers can be recognized by their smaller cross-sectional area compared with others of the same fiber type (e.g., Willemse and van den Berg, 1978), by birthdating (Alfei et al., 1994; Rowlerson et al., 1997), and by their expression of embryonic or immature myosin isotypes (Ennion et al., 1995). Regions with new muscle fibers can also be recognized by their expression of MRF genes after mature fibers have down-regulated them (Barresi et al., 2001; Steinbacher et al., 2006, 2007). The first addition of new muscle fibers occurs by a process called stratified hyperplasia, which produces layers (strata) of fibers with different cross-sectional areas. New fast muscle fibers are first added in the region between the slow and fast fibers and at the dorsal and ventral apices of the myotome, while new slow muscle fibers are initially added at the dorsal and ventral apices of the existing slow muscle monolayer (for zebrafish, see Waterman, 1969). New fast fibers in the zebrafish germinal zone are derived from the dermomyotome (Hollway et al., 2007; Stellabotte et al., 2007), and a similar origin has been proposed for pearlfish and trout, based on the position and morphology of Pax7-expressing cells (Steinbacher et al., 2006, 2007). Thus, dermomyotome cells generating fast muscle fibers must move from the outside to the inside surface of the slow muscle monolayer. In amniotes, the earliest dermomyotome cells enter the myotome by moving around the ends of the primary myotome (Gros et al., 2004). As a result, large numbers of Pax7-positive dermomyotome cells are present at the rostral, caudal, dorsomedial, and ventrolateral edges of the amniote myotome, in the dermomyotome lips. In contrast, teleost dermomyotome cells are not abundant at the corresponding edges of the myotome; Pax7-positive dermomyotome cells are specifically excluded from the rostral and caudal ends of the myotome (Steinbacher et al., 2006; Stellabotte et al., 2007). This finding suggests that teleost dermomyotome cells move from the lateral to the medial side of the superficial slow muscle fibers by inserting themselves between slow fibers and shortly thereafter elongating into the new fibers of the germinal zone (Figs. 2, 3). Further morphological and live cell imaging studies are needed to test this model.

Teleosts, including herring, pearlfish, pacu, trout, zebrafish, sea bass, and sea bream, retain an epithelial layer of undifferentiated cells on the external surface of the myotome into the early juvenile period, particularly over the dorsal and ventral apices of the myotome (Waterman, 1969; Veggetti et al., 1990; Johnston, 1993; Ramirez-Zarzosa et al., 1995; Lopez-Albors et al., 1998; Stoiber et al., 1998; Dal Pai et al., 2000; Steinbacher et al., 2006, 2007). In at least trout and zebrafish, these cells express Pax7 (Steinbacher et al., 2006; Hollway et al., 2007; Stellabotte et al., 2007); thus, we believe that these cells are part of a persistent dermomyotome, daughters of earlier dermomyotome cells, and responsible for continued growth of the myotome. Whether these cells contribute to postlarval muscle growth, or to other tissues such as the dermis or vasculature, is unknown. Teleosts continue to add new muscle fibers and new nuclei to existing fibers through at least the juvenile period (Rowlerson and Veggetti, 2001). In most teleosts, stratified growth of the myotome is followed by a period of mosaic growth, in which new muscle fibers develop interspersed between older muscle fibers, creating a mosaic of large- and small-diameter muscle fibers. In the early larval period, lineage tracing demonstrates that dermomyotome cells in zebrafish give rise to cells that enter into the myotome (Hollway et al., 2007; Stellabotte et al., 2007), these may be precursors to mosaic hyperplasia. However, lineage tracing has not been carried out to juvenile stages, when mosaic hyperplasia is prominent. Moreover, in juvenile stages, there are very few Pax7-positive cells deep within the myotome, where extensive mosaic hyperplasia and hypertrophy are occurring (Steinbacher et al., 2006; Hollway et al., 2007; Stellabotte et al., 2007). These data suggest that either the dermomyotome cells down-regulate Pax7, or a dermomyotome-independent population of cells is responsible for mosaic hyperplasia. Long-term fate mapping will resolve the lineage relationships between dermomyotome cells, the immigrating Pax7-positive cells, and the cells that contribute to mosaic hyperplasia and hypertrophy during larval and juvenile growth.

There are similarities and differences between amniotes and teleosts in the mechanism by which dermomyotome cells generate muscle fibers. In both, dermomyotome cells proliferate as Pax7-positive cells (Hammond et al., 2007), and generate both more dermomyotome cells and differentiating muscle fibers. In both amniotes and teleosts, the expansion of the primary myotome by differentiating dermomyotome cells occurs both at its dorsal and ventral apices and within the dorsoventral central domain of the

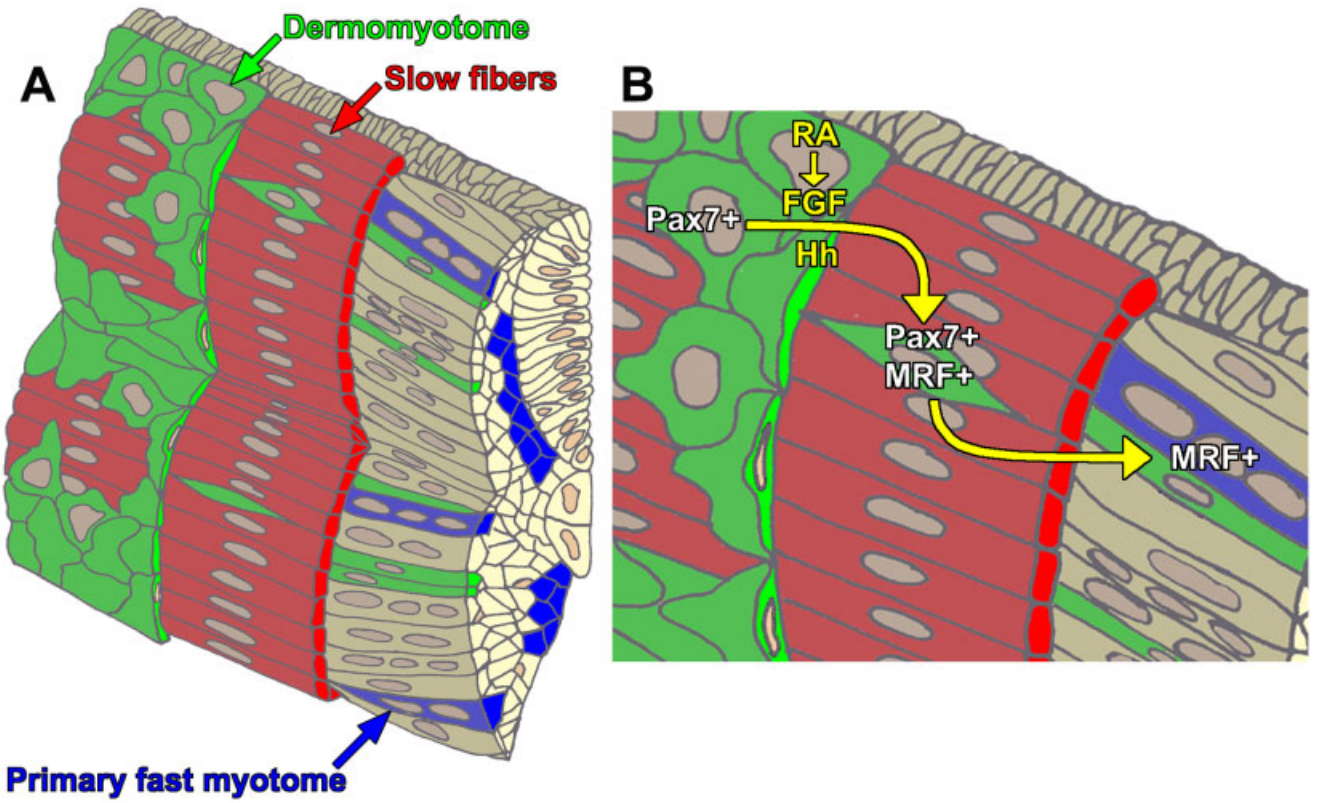

Fig. 3. Dermomyotome differentiation into muscle. **A:** A schematic of dermomyotome cells contributing to the myotome (modeled after zebrafish). Dermomyotome cells on the external surface of the somite (green) express Pax7 and are lateral to the mononucleated layer of slow muscle fibers (red). Multinucleated fast fibers (blue) are medial to slow fibers. As dermomyotome cells differentiate into muscle, they pass between slow muscle fibers and elongate to form fast fibers in lateral positions of the fast myotome. **B:** A magnified view of the path taken by cells from the dermomyotome (green) as they enter the myotome to form a fast muscle fiber (green). Hedgehog (Hh) and fibroblast growth factor (FGF) signaling molecules promote the differentiation of dermomyotome cells into muscle (Groves et al., 2005; Feng et al., 2006; Hammond et al., 2007). Retinoic acid (RA) signaling promotes the expression of FGF8, which then promotes myogenesis (Hamade et al., 2006). As cells differentiate they down-regulate Pax7 and express myogenic regulatory factors (MRFs). Elongated cells that originated in the dermomyotome occupy lateral positions in the fast myotome.

primary myotome (Kahane et al., 2002; Steinbacher et al., 2006). However, in teleosts, the first dermomyotome cells to enter the primary myotome do so by apparently migrating directly between existing superficial slow muscle fibers; in amniotes, the first dermomyotome cells enter the myotome by moving around the dorsal, ventral, rostral or caudal edges of the myotome. This difference may be primarily one of timing and degree, some dermomyotome cells in amniotes do enter the myotome by "parachuting" directly into the central domain (Gros et al., 2005). Differences in where the dermomyotome cells enter the primary myotome may result from differences in the form and function of the myotome during growth. Amniotes may have greater incorporation at the dorsal and ventral apices of the myotome than teleosts because of differences in the patterns of growth between amniote and teleost embryos, the amniote embryo may simply be taller than the teleost embryo. Moreover, while developing amniotes do not need to use their primary myotome for movement, the development of most teleosts in an external environment necessitates use of the early myotome for swimming. This finding means that myotomes in adjacent segments must be tightly apposed, potentially making it more difficult for cells to migrate around the ends of existing muscle fibers. In *Xenopus* tadpoles, which also must swim early, the dermomyotome cells have also been proposed to enter the myotome directly between superficial slow myotome fibers (Grimaldi et al., 2004), in support of the hypothesis that an early requirement for myotome functionality is incompatible with rostral and caudal dermomyotome lips. This hypothesis can be tested by examining dermomyotome cell movements in other tetrapods that do move early and in teleosts that do not move early (e.g., those with very large yolks and delayed hatching).

SIGNALING MOLECULES AND THE DERMOMYOTOME

Stromal cell-derived factor (SDF) is a secreted cytokine that plays a role in primordial germ cell migration (Raz and Reichman-Fried, 2006), lateral line migration (David et al., 2002), and melanocyte migration (Svetic et al., 2007). SDF signaling has been implicated in dermomyotome formation (Hollway et al., 2007) and myogenic differentiation (Chong et al., 2007) in zebrafish. The SDF receptor genes, *CXCR4a* and *CXCR4b* are expressed in the anterior of nascent somites (Chong et al., 2001). SDF1b is ex-

pressed in the posterior of nascent somites and then down-regulated. SDF1a expression is reported as either in the posterior (Chong et al., 2007), or the anterior (Hollway and Currie, 2005) of nascent somites. Later, SDF1a is expressed in cells on the surface of the myotome (Doitsidou et al., 2002; Li et al., 2004). Knockdown of either SDF1a, SDF1b, CXCR4a, or CXCR4b leads to a reduction in the number of dermomyotome cells expressing Pax7 (Hollway et al., 2007). The residual Pax7-positive somite cells remaining in these treated embryos are found deep and anterior within the somites, suggesting that SDF1 signaling may be necessary for their migration to the external surface of the myotome. However, the striking reduction in the number of Pax7-expressing dermomyotome cells suggests that SDF may also play a role in the initial establishment of the dermomyotome or in its maintenance. Knockdown of SDF1a or CXCR4b has also been reported to inhibit early myogenesis in zebrafish (Chong et al., 2007). Further work is needed to determine how the SDF1 signaling pathway regulates somite patterning.

Hedgehog (Hh) signaling determines the slow muscle fate of adaxial cells in zebrafish (Blagden et al., 1997; Du et al., 1997) and is required for the normal morphogenesis of the somite. Many of the components of the Hh signaling pathway have been identified by mutations in zebrafish, including the transmembrane protein Smoothened, encoded by the *slow muscle omitted* (*smo*) gene, and the Hh-activated transcription factor Gli2, encoded by the *you-too* (*yot*) gene. In the absence of Hh signaling, a primary myotome without slow muscle fibers differentiates. The initial development of the dermomyotome is apparently normal, as assayed by expression of *pax3* and *pax7* (Feng et al., 2006; Hammond et al., 2007). However, whereas wild-type embryos show a reduction in the number of dermomyotome cells as the secondary myotome forms, embryos with a loss of Hh signaling show an increase in the number of dermomyotome cells and a delay in the addition of fast muscle fibers to the primary myotome. The effect of Hh on the number of dermomyotome cells is cell-autonomous to dermomyotome cells or their precursors, its action is not mediated by other cells that respond to Hh (Feng et al., 2006). Many questions about the action of Hh are raised by these results and can be addressed in zebrafish. What cellular process in dermomyotome cells is being altered by Hh signaling? Does Hh alter the movement and/or development of ABCs into the dermomyotome, or does Hh regulate the differentiation of the dermomyotome into muscle fibers? If the latter, does Hh exert its effect on proliferation or differentiation, or both? Does Hh continue to act on the dermomyotome as the fish grows, and if so, what is the source of Hh? Pharmacological inhibition of Hh signaling can be used in other teleost species to test whether Hh also regulates dermomyotome differentiation into secondary myotome.

Fibroblast growth factor 8 (FGF8) and retinoic acid (RA) signaling also promote myogenesis in zebrafish somites. FGF8 is expressed in the anterior cells of recently formed somites, and appears to promote myogenesis from dermomyotome cells, perhaps in an autocrine manner. When FGF8 signaling is reduced during segmentation stages, the dermomyotome retains Pax3 expression and there is a reduction in myogenic differentiation (Groves et al., 2005; Hammond et al., 2007). RA has similar effects on myogenesis as FGF8. The addition of exogenous RA increases, and inhibition of RA signaling reduces MRF expression in somites. Retinoic acid also induces expansion of FGF8 expression, and the effect of RA on MRF expression is dependent on FGF8—inhibition of FGF8 signaling blocks the effect of exogenous RA (Hamade et al., 2006).

Similar signals regulate myogenic differentiation in the amniote dermomyotome (for review, see Bothe et al., this issue, pages 2397–2409). Hh, released from the notochord and floor plate, promotes myogenesis from the dermomyotome, leading to the expansion of MRF expression and a reduction of Pax3 expression (Amthor et al., 1999). FGF signaling can also promote myogenesis in amniotes and may play a role in mediating the myogenic "community effect" (Marics et al., 2002; Buckingham, 2003). RA also promotes myogenesis in amniotes (Froeschle et al., 1996; Alric et al., 1998). Whether other signals that regulate myogenic differentiation from the amniote dermomyotome, such as Wnt, BMP4/7, and Notch signaling also regulate the fates of the teleost dermomyotome remains to be determined. The dermomyotome is maintained by a balance of proliferation and differentiation. In teleosts, the extensive growth of the myotome over long larval and juvenile periods, and the likely maintenance of the dermomyotome into the juvenile period, make this balance particularly important.

MECHANISM OF CELLULAR REARRANGEMENTS IN THE SOMITE

Three successive cell rearrangements occur during the formation of the dermomyotome and its subsequent myogenic differentiation. First, the posterior cells of the epithelial somite move medial to the adaxial cells, and elongate. Second, at approximately the same time, the ABCs move laterally, to the external surface of the somite (Fig. 2A–C). These two cellular rearrangements result in a primary myotome with deep (medial) fast fibers derived from posterior cells, and superficial (lateral) slow fibers derived from medial cells (adaxial). External to this primary myotome are dermomyotome cells derived from ABCs (Fig. 2C,D). The third cell rearrangement occurs when dermomyotome cells move medial to the primary slow fibers, to develop into secondary fast fibers in the myogenic germinal zones at the lateral surface of the older fast fibers (Figs. 2C,E, 3A).

Two models for the mechanisms underlying these cellular rearrangements have been proposed. First, they may result from whole-somite rotation, the spatially and temporally coherent movement of most or all the cells in the somite (Hollway et al., 2007). Second, the rearrangements may result from the active migration of adaxial cells laterally, and/or the active migration of posterior cells and then dermomyotome cells medially (Stellabotte et al., 2007). These two models can be tested by carefully map-

ping the position and movements of many somite cells simultaneously during the period of cell rearrangements. Whole somite rotation should largely preserve cellular neighbor relationships. In contrast, if individual cells change their position relative to each other extensively, it would suggest dynamic cell rearrangements. Further information about the mechanisms of cell rearrangements should come from a greater understanding of the molecular factors promoting cell movement. Differential cell adhesion, driven by dynamic expression patterns of M- and N-Cadherin within the somite, is required for the rearrangement of slow and fast muscle precursors (Cortes et al., 2003), suggesting that cellular rearrangements within the somite, rather than a coherent whole somite rotation, underlie the cellular rearrangements.

The close correlation between the lateral movement of the slow muscle fibers of the primary myotome and the differentiation of new fast fibers medial to them raises the possibility of a causal linkage between the differentiation of fast muscle fibers and the cellular rearrangements described above (Henry and Amacher, 2004). Such a linkage is supported by observations that fast fiber myogenic gene expression and fast fiber elongation is delayed in embryos lacking Hh signaling as a result of mutations in *smoothened* (*smo*). Intriguingly, the mechanism by which Hh promotes fast muscle gene expression is different from the mechanism by which it promotes fast fiber elongation. The effect of Hh signaling on dermomyotome cell myogenic differentiation is direct, not mediated by slow muscle fibers (Feng et al., 2006). In contrast, the effect of Hh on elongation is indirect, mediated by its effect on primary slow muscle fibers (Henry and Amacher, 2004). Thus, as in chick, the primary myotome may be necessary for normal morphogenesis of later developing muscle fibers (Henry and Amacher, 2004; Kahane et al., 2007). Other mutations that disrupt slow fiber development and/or disrupt cellular rearrangements can be used to test this hypothesis. For example, mutations in the zebrafish *gli-2* (*yot*) and the *blimp-1* (*ubo*) genes lead to the loss of all primary slow fibers, but do not significantly affect the molecular differentiation of fast muscle cells from the dermomyotome (Roy et al., 2001; Baxendale et al., 2004; Feng et al., 2006). Similarly, mutations in *n-cadherin* (*parachute*) disrupt slow muscle migration, but do not disrupt fast muscle differentiation (Cortes et al., 2003; Birely et al., 2005). Examination of fast muscle cell elongation in these situations, where slow muscle is missing or cell rearrangements do not occur, will test whether the cellular rearrangements of slow fibers and fast muscle precursors play a role in promoting fast fiber elongation.

DERMOMYOTOME CONTRIBUTIONS TO APPENDICULAR AND HYPAXIAL MUSCLE

Most of the dermomyotome in teleosts contributes to axial muscle, which forms the vast majority of muscle in almost all species. However, the dermomyotome at specific anterior posterior axial levels likely contributes to the sternohyoideus muscle, pectoral fin muscle, anterior hypaxial muscle, and pelvic fin muscle. The sternohyoideus muscle in teleosts is homologous to the muscles of the tongue in amniotes (Winterbottom, 1974), and is innervated by motor neurons in the spinal cord (Schilling and Kimmel, 1997). Fate mapping will be necessary to determine whether the sternohyoideus, like the amniote tongue derives from the dermomyotome of anterior somite(s). Teleost pectoral fin muscles are derived from proliferative mesenchymal cells that enter the fin bud from a subset of anterior somites, likely in response to signals from the lateral plate (reviewed in Hollway and Currie, 2005). In zebrafish, cells from somites 2–4 contribute to the fin musculature (Neyt et al., 2000). The ventrolateral cells of these somites express c-met, the receptor for scatter factor/hepatocyte growth factor (SF/HGF); SF/HGF is expressed by the lateral plate mesenchyme. SDF/HGF and c-met are required for the migration of dermomyotome cells into the chick limb. The migration of teleost pectoral fin muscles is also dependent on SF/HGF (Haines et al., 2004). The somitic precursors to these fin muscle fibers are in the anterior of epithelial somites (Hollway et al., 2007). If these anterior cells in somites 2–4 enter first into the dermomyotome, as seems quite likely, the muscles of the anterior paired appendages in teleosts are derived from the dermomyotome, as they are in amniotes (see the review by Cole and Currie, this issue, pages 2421–2431). Pelvic fins in most teleosts develop long after the end of segmentation, during the later larval period (Grandel and Schulte-Merker, 1998). The persistence of the dermomyotome into at least juvenile stages in most teleosts (see above), allows the dermomyotome in the region of the pelvic fin to contribute muscle precursors to these appendages as well. Both pectoral and pelvic fin muscles develop in an environment composed of lateral plate-derived connective tissue (the abaxial domain, reviewed by Winslow et al., this issue, pages 2371–2381).

Zebrafish also develop a ventral, anterior body wall muscle that has been termed the posterior hypaxial muscle (Haines et al., 2004), or ventral-most hypaxial muscle (Barresi et al., 2001). This is a sheet of muscle that can be seen with myosin labeling to extend anterior from the ventral edge of somite 7 or 8 to ultimately attach to the cleithrum (Haines et al., 2004). Posterior hypaxial muscle develops from cells in the anterior of epithelial somites 5 and 6 (Hollway et al., 2007), but these cells form muscle differently than do the fin muscle precursors. The formation of these muscles appears to result from the extension of the myotome, rather than the migration of mesenchymal cells from a dermomyotome. Whether the connective tissue of this muscle is derived from somite cells or from lateral plate cells remains to be determined.

In addition to these different muscles derived from the dermomyotome at specific anterior posterior levels, the dermomyotome at all levels gives rise to axial muscle, which differentiates in an environment likely composed of somite-derived connective tissue (the primaxial domain, see review by Winslow et al., this issue, pages 2371–2381). The basis for anteroposterior differences in teleost dermomyotome cell fates is unclear. In amniotes, somites at specific anteroposterior levels have an intrinsic

predisposition to generate limb muscles (Alvares et al., 2003). However, heterotopic transplantation of equivalently staged somites has demonstrated that all somites have similar potential and that the anteroposterior specificity of dermomyotome patterning can be reprogrammed by signaling molecules in the lateral plate (Chevallier et al., 1977). In zebrafish, similar transplantation studies have demonstrated that somites become restricted in their competence to form fin muscle before the differentiation of the fin primordia (Haines et al., 2004). This finding is likely a result of anteroposterior differences in expression of the SF/HGF receptor, c-met, in the somite (Haines et al., 2004). However, heterotopic transplantation of somites in zebrafish has been done only after the lateral plate mesoderm shows region-specific gene expression (Wakahara et al., 2007). This finding raises the possibility that the somites had been restricted in their competence to form limb muscle by interactions with the lateral plate before transplantation.

DERMOMYOTOME CONTRIBUTIONS TO THE DERMIS

Some of the zebrafish dermomyotome precursors examined by lineage labeling were reported to give rise to "dermis" cells, based on their position (Hollway et al., 2007). However, as the teleost dermis has not been well characterized in any species, these results must be viewed as preliminary. A cellularized layer beneath the epidermis and disconnected from the myotome first develops during very late larval development in zebrafish (approximately 4 weeks of life; Le Guellec et al., 2004). These cells are presumed to be dermis, based solely on their position and morphology. Long-term fate mapping studies will be necessary to determine whether these cells derive from the dermomyotome, as the dermis does in amniotes (Ben-Yair and Kalcheim, 2005).

During the segmentation stages of both trout and zebrafish, several collagen genes are expressed by epidermal cells and also by cells on the surface of the myotome. These latter cells, called "dermal endothelial cells" in zebrafish (Le Guellec et al., 2004), and "dermatome" in trout (Rescan et al., 2005), are not fibroblastic cells within the extracellular matrix surrounding the somite, rather they closely resemble the *pax7*-expressing cells of the dermomyotome at this stage. In trout, although double labeling has not been done, it appears that all of the cells on the surface of the myotome at the end of segmentation period express the *col1α1* gene (Rescan et al., 2005), and most if not all of the cells on the surface of the myotome express the dermomyotome marker Pax7 (Steinbacher et al., 2007). If this is true, it would suggest that dermomyotome cells express some of the same collagen genes as the epidermis and later dermis. In zebrafish, it is not clear whether cells expressing *col1a2* (Le Guellec et al., 2004), are the same as or distinct from the *pax7*-expressing dermomyotome (Hammond et al., 2007). If *pax7* positive dermomyotome cells also express *collagen*, this may indicate that these dermomyotome cells are beginning to differentiate into dermis, or it may simply be that the cells of the dermomyotome remain multipotent, but contribute to the formation of the acellular connective tissue between the myotome and the epidermis. The identification of cell-specific molecular markers and further fate mapping studies will clarify the relationship between the dermomyotome, the dermal endothelial cells, and the dermis in teleosts.

PERSPECTIVES

The teleost dermomyotome shares many features with that of amniotes: it forms shortly after segmentation, it consists of an epithelium on the external surface of the primary myotome, it expresses genes homologous to those expressed in amniotes, it gives rise to muscle fibers that become part of the myotome or the paired appendages, and it is regulated by homologous signaling molecules. Paradoxically, the two biggest differences between teleost and amniote dermomyotome relate to the formation of the dermomyotome and to the dissolution of the dermomyotome. Unlike the chick and mouse dermomyotome, the teleost dermomyotome forms from the anterior of newly formed somites, and unlike the chick dermomyotome, the earliest teleost dermomyotome cells do not apparently migrate around rostral and caudal lips to enter the myotome. The striking similarities of the dermomyotome itself suggest that it is highly conserved, even while its mode of formation and mode of dispersal are not. There are several possible reasons for the conservation of the dermomyotome. First, it may provide a structure required for cell–cell interactions that regulate the fate of myogenic and dermal precursors. Second, it may provide a substrate required by surrounding cells such as lateral line or neural crest, which may depend on the epithelial cell layer of the dermomyotome for their normal development. Finally, the dermomyotome may provide a structure that mechanically constrains the embryo before the development of more mature connective tissue and epidermis.

The recognition that teleosts have a dermomyotome with many shared features of the amniote dermomyotome opens up a new experimental system for understanding the dermomyotome. The embryological and genetic advantages of zebrafish that have proven to be so powerful for understanding segmentation (Holley, 2007) and myogenesis (Hollway and Currie, 2005) can be now applied to uncovering the mechanism of dermomyotome formation and its differentiation into specialized cell types. Other teleosts, which grow more slowly, and/or to a larger final size, offer opportunities to address the role of hormones, diet, and environmental variables on dermomyotome development. Lessons learned in teleosts about the cellular and molecular bases for multiple waves of myogenesis can then be applied to amniote dermomyotome differentiation.

In addition to the utility of teleosts as a model for amniote dermomyotome, teleosts provide an enormous resource for comparative and evolutionary studies of dermomyotome development. The over 26,000 different extant species of teleosts display an astonishing variety of adult forms (Nelson, 2006). Many of the defining features of adult teleosts are the shape and size of their axial musculature, which determines to a large extent the shape and size of their trunk

and tail. The dermomyotome of very few species has been described in any way, and only in zebrafish has experimental embryology and genetics been used to study the dermomyotome. The great diversity of shapes and life histories within teleosts provides a valuable resource for understanding how evolutionary changes in dermomyotome formation and differentiation can alter the sizes and shapes of the resulting animal.

ACKNOWLEDGMENTS

We thank Sara Patterson for helpful comments on the manuscript. S.H.D. was funded by the NIH.

REFERENCES

Afonin B, Ho M, Gustin JK, Melody-Kapella C, Domingo CR. 2006. Cell behaviors associated with somite segmentation and rotation in Xenopus laevis. Dev Dyn 235:3268–3279.

Alfei L, Onali A, Spano L, Colombari PT, Altavista PL, De Vita R. 1994. PCNA/cyclin expression and BrdU uptake define proliferating myosatellite cells during hyperplastic muscle growth of fish (Cyprinus carpio L.). Eur J Histochem 38:151–162.

Alric S, Froeschle A, Piquemal D, Carnac G, Bonnieu A. 1998. Functional specificity of the two retinoic acid receptor RAR and RXR families in myogenesis. Oncogene 16:273–282.

Alvares LE, Schubert FR, Thorpe C, Mootoosamy RC, Cheng L, Parkyn G, Lumsden A, Dietrich S. 2003. Intrinsic, Hox-dependent cues determine the fate of skeletal muscle precursors. Dev Cell 5:379–390.

Amthor H, Christ B, Patel K. 1999. A molecular mechanism enabling continuous embryonic muscle growth - a balance between proliferation and differentiation. Development 126:1041–1053.

Barresi MJ, D'Angelo JA, Hernandez LP, Devoto SH. 2001. Distinct mechanisms regulate slow-muscle development. Curr Biol 11:1432–1438.

Baxendale S, Davison C, Muxworthy C, Wolff C, Ingham PW, Roy S. 2004. The B-cell maturation factor Blimp-1 specifies vertebrate slow-twitch muscle fiber identity in response to Hedgehog signaling. Nat Genet 36:88–93.

Ben-Yair R, Kalcheim C. 2005. Lineage analysis of the avian dermomyotome sheet reveals the existence of single cells with both dermal and muscle progenitor fates. Development 132:689–701.

Birely J, Schneider VA, Santana E, Dosch R, Wagner DS, Mullins MC, Granato M. 2005. Genetic screens for genes controlling motor nerve-muscle development and interactions. Dev Biol 280:162–176.

Blagden CS, Currie PD, Ingham PW, Hughes SM. 1997. Notochord induction of zebrafish slow muscle mediated by Sonic hedgehog. Genes Dev 11:2163–2175.

Borycki AG, Mendham L, Emerson CP Jr. 1998. Control of somite patterning by Sonic hedgehog and its downstream signal response genes. Development 125:777–790.

Brand-Saberi B, Christ B. 2000. Evolution and development of distinct cell lineages derived from somites. Curr Top Dev Biol 2000:1–42.

Buckingham M. 2003. How the community effect orchestrates muscle differentiation. Bioessays 25:13–16.

Chevallier A, Kieny M, Mauger A. 1977. Limb-somite relationship: origin of the limb musculature. J Embryol Exp Morphol 41:245–258.

Chong SW, Emelyanov A, Gong Z, Korzh V. 2001. Expression pattern of two zebrafish genes, cxcr4a and cxcr4b. Mech Dev 109:347–354.

Chong SW, Nguyet LM, Jiang YJ, Korzh V. 2007. The chemokine, Sdf-1, and its receptor, Cxcr4, are required for formation of muscle in zebrafish. BMC Dev Biol 7:54.

Cole NJ, Hall TE, Martin CI, Chapman MA, Kobiyama A, Nihei Y, Watabe S, Johnston IA. 2004. Temperature and the expression of myogenic regulatory factors (MRFs) and myosin heavy chain isoforms during embryogenesis in the common carp Cyprinus carpio L. J Exp Biol 207:4239–4248.

Cortes F, Daggett D, Bryson-Richardson RJ, Neyt C, Maule J, Gautier P, Hollway GE, Keenan D, Currie PD. 2003. Cadherin-mediated differential cell adhesion controls slow muscle cell migration in the developing zebrafish myotome. Dev Cell 5:865–876.

Dal Pai V, Dal Pai-Silva M, Carvalho ED, Fujihara CY, Gregorio EA, Curi PR. 2000. Morphological, histochemical and morphometric study of the myotomal muscle tissue of the pacu (Piaractus mesopotamicus Holmberg 1887: Serrasalminae, Characidae, Teleostei). Anat Histol Embryol 29:283–289.

Dal Pai-Silva M, Freitas EMS, Dal Pai V, Rodrigues AD. 2003. Morphological and histochemical study of the myotomal muscle in pacu (Piaractus mesopotamicus Holmberg, 1887) during the initial growth phases. Arch Fish Mar Res 50:149–160.

David NB, Sapede D, Saint-Etienne L, Thisse C, Thisse B, Dambly-Chaudiere C, Rosa FM, Ghysen A. 2002. Molecular basis of cell migration in the fish lateral line: role of the chemokine receptor CXCR4 and of its ligand, SDF1. Proc Natl Acad Sci U S A 99:16297–16302.

Delalande JM, Rescan PY. 1999. Differential expression of two nonallelic MyoD genes in developing and adult myotomal musculature of the trout (Oncorhynchus mykiss). Dev Genes Evol 209:432–437.

Denetclaw WF Jr, Christ B, Ordahl CP. 1997. Location and growth of epaxial myotome precursor cells. Development 124:1601–1610.

Devoto SH, Stoiber W, Hammond CL, Steinbacher P, Haslett JR, Barresi MJ, Patterson SE, Adiarte EG, Hughes SM. 2006. Generality of vertebrate developmental patterns: evidence for a dermomyotome in fish. Evol Dev 8:101–110.

Doitsidou M, Reichman-Fried M, Stebler J, Koprunner M, Dorries J, Meyer D, Esguerra CV, Leung T, Raz E. 2002. Guidance of primordial germ cell migration by the chemokine SDF-1. Cell 111:647–659.

Du SJ, Devoto SH, Westerfield M, Moon RT. 1997. Positive and negative regulation of muscle cell identity by members of the hedgehog and TGF-beta gene families. J Cell Biol 139:145–156.

Ehrlich R. 1875. Ueber den peripheren Theil der Urwirbel. Arch Mikroskop Anat 78:313–327.

Eloy-Trinquet S, Nicolas JF. 2002. Cell coherence during production of the presomitic mesoderm and somitogenesis in the mouse embryo. Development 129:3609–3619.

Ennion S, Gauvry L, Butterworth P, Goldspink G. 1995. Small-diameter white myotomal muscle fibres associated with growth hyperplasia in the carp (Cyprinus carpio) express a distinct myosin heavy chain gene. J Exp Biol 198:1603–1611.

Feng X, Adiarte EG, Devoto SH. 2006. Hedgehog acts directly on the zebrafish dermomyotome to promote myogenic differentiation. Dev Biol 300:736–746.

Froeschle A, Carnac G, Alric S, Montarras D, Pinset C, Rochette-Egly C, Bonnieu A. 1996. RXR alpha is essential for mediating the all-trans retinoic acid-induced growth arrest of C2 myogenic cells. Oncogene 12:411–421.

Gadow H, Abbot EC. 1895. On the evolution of the vertebral column of fishes. Philos Trans R Soc Lond B 186:163–221.

Grandel H, Schulte-Merker S. 1998. The development of the paired fins in the zebrafish (Danio rerio). Mech Dev 79:99–120.

Grimaldi A, Tettamanti G, Martin BL, Gaffield W, Pownall ME, Hughes SM. 2004. Hedgehog regulation of superficial slow muscle fibres in Xenopus and the evolution of tetrapod trunk myogenesis. Development 131:3249–3262.

Gros J, Scaal M, Marcelle C. 2004. A two-step mechanism for myotome formation in chick. Dev Cell 6:875–882.

Gros J, Manceau M, Thome V, Marcelle C. 2005. A common somitic origin for embryonic muscle progenitors and satellite cells. Nature 435:954–958.

Groves JA, Hammond CL, Hughes SM. 2005. Fgf8 drives myogenic progression of a novel lateral fast muscle fibre population in zebrafish. Development 132:4211–4222.

Haines L, Neyt C, Gautier P, Keenan DG, Bryson-Richardson RJ, Hollway GE, Cole NJ, Currie PD. 2004. Met and Hgf signaling controls hypaxial muscle and

lateral line development in the zebrafish. Development 131:4857–4869.

Hamade A, Deries M, Begemann G, Bally-Cuif L, Genet C, Sabatier F, Bonnieu A, Cousin X. 2006. Retinoic acid activates myogenesis in vivo through Fgf8 signalling. Dev Biol 289:127–140.

Hammond CL, Hinits Y, Osborn DP, Minchin JE, Tettamanti G, Hughes SM. 2007. Signals and myogenic regulatory factors restrict pax3 and pax7 expression to dermomyotome-like tissue in zebrafish. Dev Biol 302:504–521.

Henry CA, Amacher SL. 2004. Zebrafish slow muscle cell migration induces a wave of fast muscle morphogenesis. Dev Cell 7:917–923.

Holley SA. 2007. The genetics and embryology of zebrafish metamerism. Dev Dyn 236:1422–1449.

Hollway G, Currie P. 2005. Vertebrate myotome development. Birth Defects Res C Embryo Today 75:172–179.

Hollway GE, Bryson-Richardson RJ, Berger S, Cole NJ, Hall TE, Currie PD. 2007. Whole-somite rotation generates muscle progenitor cell compartments in the developing zebrafish embryo. Dev Cell 12:207–219.

Hopwood ND, Pluck A, Gurdon JB. 1991. Xenopus Myf-5 marks early muscle cells and can activate muscle genes ectopically in early embryos. Development 111: 551–560.

Hopwood ND, Pluck A, Gurdon JB, Dilworth SM. 1992. Expression of XMyoD protein in early Xenopus laevis embryos. Development 114:31–38.

Johnston IA. 1993. Temperature Influences Muscle Differentiation and the Relative Timing of Organogenesis in Herring (Clupea-Harengus) Larvae. Mar Biol 116:363–379.

Kaehn K, Jacob HJ, Christ B, Hinrichsen K, Poelmann RE. 1988. The onset of myotome formation in the chick. Anat Embryol (Berl) 177:191–201.

Kaestner S. 1892. Ueber die allgemeine Entwicklung der Rumpf- und Schwanzmusculatur bei Wirbelthieren. Mit besonderer Berueecksichtigung der Selachier. Arch Anat Entwickelungsgesch 153–222.

Kahane N, Kalcheim C. 1998. Identification of early postmitotic cells in distinct embryonic sites and their possible roles in morphogenesis. Cell Tissue Res 294: 297–307.

Kahane N, Cinnamon Y, Kalcheim C. 1998. The origin and fate of pioneer myotomal cells in the avian embryo. Mech Dev 74: 59–73.

Kahane N, Cinnamon Y, Kalcheim C. 2002. The roles of cell migration and myofiber intercalation in patterning formation of the postmitotic myotome. Development 129:2675–2687.

Kahane N, Ben-Yair R, Kalcheim C. 2007. Medial pioneer fibers pattern the morphogenesis of early myoblasts derived from the lateral somite. Dev Biol 305: 439–450.

Keller R. 2000. The origin and morphogenesis of amphibian somites. Curr Top Dev Biol 47:183–246.

Kusakabe R, Kuratani S. 2005. Evolution and developmental patterning of the vertebrate skeletal muscles: perspectives from the lamprey. Dev Dyn 234:824–834.

Le Guellec D, Morvan-Dubois G, Sire JY. 2004. Skin development in bony fish with particular emphasis on collagen deposition in the dermis of the zebrafish (Danio rerio). Int J Dev Biol 48:217–231.

Li Q, Shirabe K, Kuwada JY. 2004. Chemokine signaling regulates sensory cell migration in zebrafish. Dev Biol 269:123–136.

Lillie FR. 1919. The development of the chick: an introduction to embryology. New York: Henry Holt and Company.

Lopez-Albors O, Gil F, Ramirez-Zarzosa G, Vazquez JM, Latorre R, Garcia-Alcazar A, Arencibia A, Moreno F. 1998. Muscle development in gilthead sea bream (Sparus aurata, L.) and sea bass (Dicentrarchus labrax, L.): further histochemical and ultrastructural aspects. Anat Histol Embryol 27:223–229.

Marics I, Padilla F, Guillemot JF, Scaal M, Marcelle C. 2002. FGFR4 signaling is a necessary step in limb muscle differentiation. Development 129:4559–4569.

Maurer F. 1894. Die Elements der Rumpfmuskelatur bei Cyclostomen und Loheren Wirbeltieren. Ein Beitrag sur Phylogenie des quergestreiften Muskelfaser. Morphol Jahrbuch 21:473–619.

Nelson JS. 2006. Fishes of the world. New York: John Wiley and Sons.

Neyt C, Jagla K, Thisse C, Thisse B, Haines L, Currie PD. 2000. Evolutionary origins of vertebrate appendicular muscle. Nature 408:82–86.

O'Connell CP. 1981. Development of organ systems in the northern anchovy, *Engraulis mordax*, and other teleosts. Am Zool 21:429–446.

Ott MO, Bober E, Lyons G, Arnold H, Buckingham M. 1991. Early expression of the myogenic regulatory gene, *myf-5*, in precursor cells of skeletal muscle in the mouse embryo. Development 111: 1097–1107.

Pownall ME, Emerson CP Jr. 1992. Sequential activation of three myogenic regulatory genes during somite morphogenesis in quail embryos. Dev Biol 151: 67–79.

Ramirez-Zarzosa G, Gil F, Latorre R, Ortega A, Garcia-Alcaraz A, Abellan E, Vazquez JM, Lopez-Albors O, Arencibia A, Moreno F. 1995. The larval development of lateral musculature in gilthead sea bream Sparus-Aurata and sea bass Dicentrarchus-Labrax. Cell Tissue Res 280:217–224.

Raz E, Reichman-Fried M. 2006. Attraction rules: germ cell migration in zebrafish. Curr Opin Genet Dev 16:355–359.

Rescan PY. 2005. Muscle growth patterns and regulation during fish ontogeny. Gen Comp Endocrinol 142:111–116.

Rescan PY, Collet B, Ralliere C, Cauty C, Delalande JM, Goldspink G, Fauconneau B. 2001. Red and white muscle development in the trout (Oncorhynchus mykiss) as shown by in situ hybridisation of fast and slow myosin heavy chain transcripts. J Exp Biol 204:2097–2101.

Rescan PY, Ralliere C, Chauvigne F, Cauty C. 2005. Expression patterns of collagen I (alpha1) encoding gene and muscle-specific genes reveal that the lateral domain of the fish somite forms a connective tissue surrounding the myotome. Dev Dyn 233:605–611.

Rowlerson A, Veggetti A. 2001. Cellular mechanisms of post-embryonic muscle growth in aquaculture species. In: Johnston IA, editor. Muscle development and growth. San Diego: Academic Press. p 103–140.

Rowlerson A, Radaelli G, Mascarello F, Veggetti A. 1997. Regeneration of skeletal muscle in two teleost fish: Sparus aurata and Brachydanio rerio. Cell Tissue Res 289:311–322.

Roy S, Wolff C, Ingham PW. 2001. The u-boot mutation identifies a Hedgehog-regulated myogenic switch for fiber-type diversification in the zebrafish embryo. Genes Dev 15:1563–1576.

Scaal M, Wiegreffe C. 2006. Somite compartments in anamniotes. Anat Embryol (Berl) 211:9–19.

Schilling TF, Kimmel CB. 1997. Musculoskeletal patterning in the pharyngeal segments of the zebrafish embryo. Development 124:2945–2960.

Selleck MA, Stern CD. 1991. Fate mapping and cell lineage analysis of Hensen's node in the chick embryo. Development 112:615–626.

Steinbacher P, Haslett JR, Six M, Gollmann HP, Sanger AM, Stoiber W. 2006. Phases of myogenic cell activation and possible role of dermomyotome cells in teleost muscle formation. Dev Dyn 235: 3132–3143.

Steinbacher P, Haslett JR, Obermayer A, Marschallinger J, Bauer HC, Sanger AM, Stoiber W. 2007. MyoD and Myogenin expression during myogenic phases in brown trout: a precocious onset of mosaic hyperplasia is a prerequisite for fast somatic growth. Dev Dyn 236:1106–1114.

Stellabotte F, Dobbs-McAuliffe B, Fernandez DA, Feng X, Devoto SH. 2007. Dynamic somite cell rearrangements lead to distinct waves of myotome growth. Development 134:1253–1257.

Stern CD, Canning DR. 1990. Origin of cells giving rise to mesoderm and endoderm in chick embryo. Nature 343: 273–275.

Stickney HL, Barresi MJ, Devoto SH. 2000. Somite development in zebrafish. Dev Dyn 219:287–303.

Stoiber W, Haslett JR, Goldschmid A, Sanger AM. 1998. Patterns of superficial fibre formation in the European pearlfish (Rutilus frisii meidingeri) provide a general template for slow muscle development in teleost fish. Anat Embryol (Berl) 197:485–496.

Sunier ALJ. 1911. Les premiers stades de la differentiation interne du myotome et la formation des elements sclerotomatiques chez les acraniens, les Selaciens, et les Teleosteens. Tijdschrifts Nederlandsche Dierkunkige Vereniging 12:75–181.

Svetic V, Hollway GE, Elworthy S, Chipperfield TR, Davison C, Adams RJ, Eisen JS, Ingham PW, Currie PD, Kelsh RN. 2007. Sdf1a patterns zebrafish melanophores and links the somite and melanophore pattern defects in choker mutants. Development 134:1011–1022.

Temple GK, Cole NJ, Johnston IA. 2001. Embryonic temperature and the relative timing of muscle-specific genes during development in herring (Clupea harengus L.). J Exp Biol 204:3629–3637.

Thisse C, Thisse B, Schilling TF, Postlethwait JH. 1993. Structure of the zebrafish *snail1* gene and its expression in wild-type, *spadetail* and *no tail* mutant embryos. Development 119:1203–1215.

Veggetti A, Mascarello F, Scapolo PA, Rowlerson A. 1990. Hyperplastic and hypertrophic growth of lateral muscle in Dicentrarchus labrax (L.). An ultrastructural and morphometric study. Anat Embryol (Berl) 182:1–10.

Venters SJ, Thorsteinsdottir S, Duxson MJ. 1999. Early development of the myotome in the mouse. Dev Dyn 216:219–232.

Wagner J, Schmidt C, Nikowits W Jr, Christ B. 2000. Compartmentalization of the somite and myogenesis in chick embryos are influenced by wnt expression. Dev Biol 228:86–94.

Wakahara T, Kusu N, Yamauchi H, Kimura I, Konishi M, Miyake A, Itoh N. 2007. Fibin, a novel secreted lateral plate mesoderm signal, is essential for pectoral fin bud initiation in zebrafish. Dev Biol 303:527–535.

Waterman RE. 1969. Development of the lateral musculature in the teleost, *Brachydanio rerio*: a fine structural study. Am J Anat 125:457–493.

Weinberg ES, Allende ML, Kelly CS, Abdelhamid A, Andermann P, Doerre G, Grunwald DJ, Riggleman B. 1996. Developmental regulation of zebrafish *MyoD* in wild-type, *no tail*, and *spadetail* embryos. Development 122:271–280.

Willemse JJ, van den Berg PG. 1978. Growth of striated muscle fibres in the M. lateralis of the European eel Anguilla anguilla (L.) (Pisces, Teleostei). J Anat 125:447–460.

Winterbottom R. 1974. Descriptive synonymy of striated muscles of teleostei. Proc Acad Nat Sci Phila 125:225–317.

Williams LW. 1910. The somites of the chick. Am J Anat 11:55–100.

Williams BA, Ordahl CP. 1997. Emergence of determined myotome precursor cells in the somite. Development 124:4983–4997.

Xu Y, He J, Wang X, Lim TM, Gong Z. 2000. Asynchronous activation of 10 muscle-specific protein (MSP) genes during zebrafish somitogenesis. Dev Dyn 219: 201–215.

Zhang Y, Tan X, Zhang PJ, Xu Y. 2006. Characterization of muscle-regulatory gene, MyoD, from flounder (Paralichthys olivaceus) and analysis of its expression patterns during embryogenesis. Mar Biotechnol (NY) 8:139–148.