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Somites and Head Mesoderm Arise From Somitomeres

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Abstract. Somitomeres form during gastrulation as metameric units in order from the tip of the head to the tip of the tail. Somitomeres are initially circular bilaminar domains of paraxial mesodermal mesenchymal cells, and most condense to become somites, but the cranial (sub- and preotic) somitomeres expand as the associated brain parts expand and thus do not form somites. Compared to lamprey, shark and newt, the amniotes and a teleost have doubled the numbers of cranial somitomeres, except for the first one, which may be an adaptation of the paraxial mesoderm to keep up with the rapidly expanding brains of these taxa. Paraxial mesodermal cells in the crotches between somitomeres likely form angioblasts which contribute to intersegmental and other blood vessels. Some people deny somitomeres and here for the first time I answer some of these criticisms. Gene expression patterns suggest that the files of presomitic somitomeres are being patterned in the somite pattern; however, molecular studies have not yet fully accounted for the most-posterior somitomeres. Also, the right genes have not yet been examined at the right times to see the metameric pattern of the cranial somitomeres. Head and tail are induced by different sets of gene products and their networks of interactions. The overlapping of these head-tail induction and patterning events likely produce the hind brain and trunk and their associated mesodermal segments in vertebrates.

1. Introduction

Somites, which form many segmented parts of the body, emerge from the paraxial mesoderm of the tail, trunk and posterior reaches of the head. Somites, in turn, organise the nervous system to form segmental nerves.

Segmentation of the cranial parts of the head, from the anterior tip to beneath the otocyst, has been contentious for about 200 years. With the discovery of the morphological units called somitomeres [1], it became clear that the entire paraxial mesoderm of head, trunk and tail forms a metameric pattern of somitomeres during gastrulation, beginning at the tip of the head and proceeding in order to the tip of the tail [2-6].

Somitomeres are groups of paraxial mesenchymal cells organised into circular bilaminar domains that arise as expansion figures. Initially, the newly formed somitomeres have lateral borders that coincide with the lateral borders of the neural plate which overlies them. When somitomeric units condense enough to form clefts between themselves, they are called somites.

In taxa such as amniotes in which brains enlarge considerably, the pre- and subotic somitomeres (henceforth referred to as 'cranial somitomeres') continue to expand as the brain expands and do not form large clefts between the metameric units. However,

posterior to the otocyst, somitomeres progressively condense during neurulation to form somites.

In taxa in which brain expansion is moderate or minimal, such as lampreys, sharks and amphibia, the cranial somitomeres expand less and retain a more conspicuous metameric appearance.

Noden [7] and others have shown that the cranial somitomeres differentiate into the same tissues as are formed by somites, such as voluntary muscles, bones and vascular endothelial cells.

Each somite in the trunk and tail condenses from the most-rostral somitomere of the files of somitomeres that compose the segmental plate (or presomitic mesoderm). The progressive condensation and epithelialisation of somitomeres in the segmental plate is well documented by observations and experiments [1,2,8-10]. Experimental studies also indicate that each somitomere of the segmental plate eventually forms a somite [11,12].

Recently formed somitomeres are bilayered, concave or convex discs, and are best seen with stereo scanning electron microscopy (SEM). Visualisation of these discs requires removal of the ectoderm or the endoderm after partial fixation in order to uncover the paraxial mesoderm, the washing away of extracellular matrix to reveal the cell processes of the somitomeres, then completion of fixation and choosing of appropriate tail angles to take stereo SEM's. Avian somitomeres are best described, and somitomeres were first discovered in the chick embryo in 1979 by Meier [11].

Spratt [13,15] defined "somite-forming centers" in the chick embryo on each side of the primitive streak just 0.05 mm posterior to Hensen's node. When the primitive streak begins to regress, Spratt's somite-forming centers coincide with the positions in which somitomeres first appear. However, a few of the most-rostral somitomeres and the prechordal plate are established during primitive streak elongation and thus do not fit this rule [15,16].

A study of thick plastic sections and transmission electron micrographs of the prospective third (occipital) somite of the chick embryo showed cells emerging from the primitive streak and contributing to the paraxial mesoderm. Some paraxial mesenchymal cells attach to the overlying prospective ectoderm and others orient against the endoderm. The cells hanging from the neural ectoderm attach either to the basement membrane or often directly to the ectodermal cells, usually with focal tight junctions. The cells adjacent to the endoderm most often lie flat on their sides. The entire somitomere extends laterally to the boundary between neural and non-neural ectoderm. As the neural plate contracts toward the midline, the somitomere condenses with it, keeping its lateral extent coincident with that of the neural plate [17].

In a chick embryo, the primitive streak regresses through the length of the trunk and Hensen's node is then incorporated into the tail bud. As the tail bud elongates, files of somitomeres are formed in the tail posterior to the last trunk somite [18]. Bellairs asked how the process of segmentation into somites is terminated in the chick tail and found that cell death stops the conversion of somitomeres into somites [18].

2. The Order in Which Somitomeres Form

The work of Meier [1,14] made it clear for the chick embryo that somitomeres and the somites to which they give rise are formed in strict cranial to caudal order. The first two pairs of cranial somitomeres are formed by the time the primitive streak is fully elongated (stage 4), and the rest form successively as the streak regresses. In more basal vertebrate taxa, the order of formation of somites is more complicated.

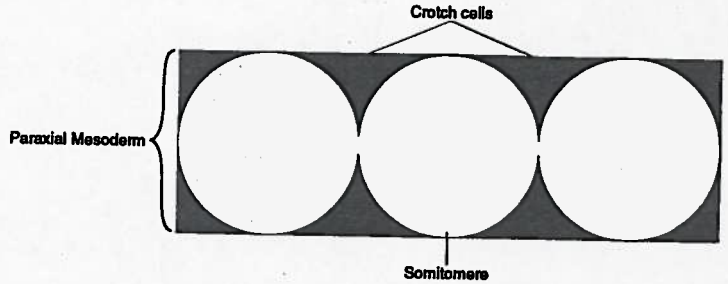

Fig. 1. This diagram shows how circular somitomeres and the crotch cells between them fit into a rectangle of paraxial mesoderm. If one subtracts the total areas of the circular somitomeres from the total area of the paraxial mesoderm, the area remaining is that occupied by crotch cells, which is 21.5% of the total area.

For example, in a newt (*Taricha torosa*), at the so-called one somite stage which is neurula stage 17, there are actually more than a dozen pairs of somitomeres aligned randomly from one end of the embryo to the other, and the "first" somite is segment number seven, the first trunk segment. The head at that time has six somitomeres, and two (the fifth and sixth segments) are destined to condense into occipital somites. Several somitomeres are formed caudal to the "first somite" and they will become trunk somites. When viewed from the lateral surface, only the seventh segments has defined clefts cranially and caudally. However, when viewed from the dorsal surface (after removal of the neural plate), or from the ventral surface (after removal of the neural plate), or from the ventral surface (after removal of the endoderm), the sixth somitomere already has clefts formed both cranially and caudally and the fifth somitomere thus has a caudal cleft and also has an incipient cranial cleft. If one judges only by the lateral clefts, the order of appearance of somites in this newt is 7, 6, 5, 8, 9, etc. [19].

3. Some Vascular Endothelial Cells Arise From Paraxial Mesoderm

Paraxial mesoderm consists of rectangular areas of mesenchymal tissue lateral to each side of the notochord. Somitomeres are circular domains whose lateral and medial boundaries are coincident with the same boundaries of the paraxial mesoderm. Circular domains of cells fitted into a rectangle leave many cells that are not within the circular domains. Simple geometry indicates that about 21.5% of the cells are in the crotches between the somitomeres (Fig. 1). Jacobson and Meier [19] suggested that these cells are largely prospective vascular endothelial cells (angioblasts). These crotches of cells are present between cranial somitomeres as well as between somitomeres in the segmental plate (presomitic mesoderm). An example from the cranial somitomeres of a newt is illustrated in Fig. 2. These extra-somitomeric paraxial cells in the brain region probably contribute many of the angioblasts that form networks of blood vessels around the brain. In mouse embryos, organising angioblasts may mimic the pattern of the underlying somitomeric cells (Fig. 3). Noden [7] discusses the origin of angioblasts from the paraxial mesoderm.

Marjorie England [20] has demonstrated the existence of intersegmental arteries between somitomeres within the entire segmental plate of chick embryos, both by injecting ink into the dorsal aorta, and by scanning electron microscopy (see her Fig. 5). These intersegmental vessels are quite obviously in the ventral crotches between somito-

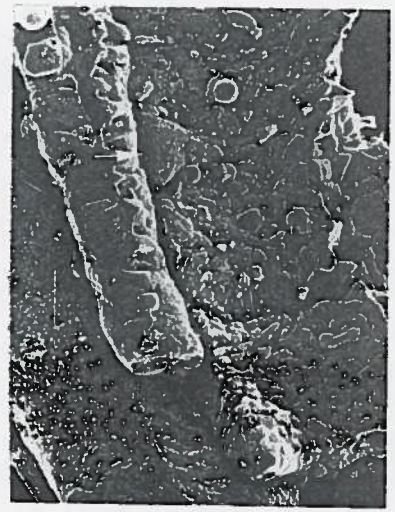

Fig. 2. SEM of a ventral view of somitomeres 4, 5 and 6 (from top down at the right) of a new embryo at the one somite stage (stage 17). The notochord is to the left. The white arrow on the notochord points to a triangular crotch of cells between somitomeres 4 and 5. Most crotch cells likely become angioblasts. (From [19], their Fig. 11.)

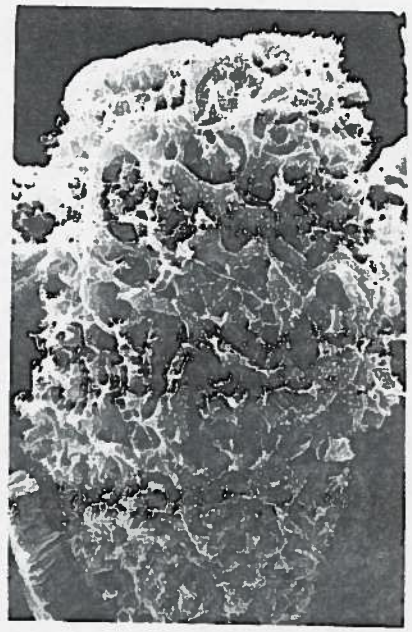

Fig. 3. SEM of a dorsal view of the left file of cranial somitomeres of a mouse embryo (neural tissue removed). At the top, only the back edge of somitomere 1 is seen. This somitomere is bent away by the forming cranial flexure. Somitomere 2 is face on and on its surface angioblasts have organised into a pattern of vessels that mimic the concentric and radial pattern of somitomere cells beneath. (From [33], their Fig. 22.)

meres, should it should be clear that the boundaries between somitomeres have a segmental meaning and the cells in the crotches likely contributed angioblasts (vascular endothelial cells) to form these vessels

Cleaver and Krieg [21] identified angioblasts with *flk-1* expression at the ventral edge of somites of *Xenopus*. These cells migrated to the midline along a concentration gradient of the diffusible form of vascular endothelial growth factor which is emitted by the endodermal hypochord lying beneath the notochord. At the midline the angioblasts form the dorsal aorta.

There are many studies that demonstrate that vascular endothelial cells can arise from somites, for example, Cox and Poole [22] found that up to 15% of the cells of a somite gave rise to angioblasts in cultures of dissociated somitic mesoderm, and that could be raised to 47% by adding FGF-2 to the culture medium.

4. Molecular Expression Patterns are Defining Somitomeres

Besides the many observational and experimental studies already cited that demonstrate that somitomeres of the segmental plate already show the meristic pattern for the future somites, an increasing number of molecular studies indicate that somitomere boundaries coincide with somite boundaries [23,24]. Fig. 4 shows ten such studies. The molecular studies so far suggest that the prospective boundaries between future somites as well as the anterior and posterior compartments with the somites become established during the period when the somites are still somitomeres. At a morphological level, even the most-recently formed (and thus most posterior) somitomere often has a line of cell processes that divides the somitomere into anterior and posterior parts which likely presage such compartments [11].

Still more patterns of segmental gene expression are being discovered in the presomitic mesoderm, so the genetic story is incomplete. When all the players are found, the network of gene activities that segments the mesoderm will be more complete. Tam *et al.* [23,24] review the molecular evidence and present partial scenarios for how the genes are thought to be functioning. More recent studies (eg. [25,26]) have introduced additional genes active in the presomitic mesoderm and advanced models for their interactions. However, these studies fail to account for the posterior extent of somitomeres in the presomitic mesoderm so the story remains incomplete.

I know of no studies in which molecular expression patterns coincide with cranial somitomeres. The molecular processes which begin with signalling from endoderm (from "Nieuwkoop's center") that induce paraxial mesoderm are still incompletely known [27], but it is apparent that the head mesoderm results from the activities of molecular networks that differ from those that produce trunk and tail mesoderm. It seems most likely that the somitomeres of the head will be defined eventually by different sets of molecular expressions than those that define the segments of the trunk and tail, and these expression patterns are likely to occur at earlier stages since head segments form first. Since cranial somitomeres expand, the patterns of molecular expression are likely to be diffuse as well and perhaps more difficult to visualise without removing overlying or underlying tissues. Cranial somitomeres likely are the product largely of the head inducers, and trunk and tail somitomeres and somites largely of the tail inducers. Between, the occipital somitomeres and somites are likely induced by a combination of head and tail inductors. Lipton and Jacobson [17] noted that the development of the occipital somites differs from most posterior somites.

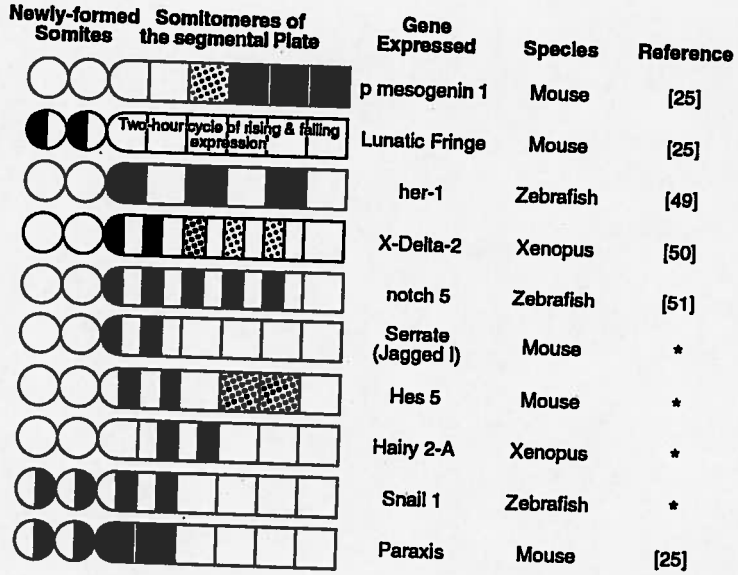

Fig. 4. Examples of gene expression patterns in presomitic mesoderm and recently formed somites. The segmental plates shown here are subdivided into six somitomeres. The segmental plate of mouse contains 5 to 6 somitomeres, and *Xenopus* has 5 to 7. Somitomeres have not been described for Zebrafish, but another teleost, the Medaka, has 10 somitomeres in its presomitic mesoderm [34]. It is clear that the patterns of gene expression in the presomitic mesoderm occur within somitomeres, or within anterior or posterior halves of somitomeres. The patterns as presented are mostly from [24], [25].

5. A Comparative Look at the Cranial Somitomeres

The disagreement as to whether the head is segmented should have ended with the discovery of cranial somitomeres in six classes of vertebrates. As stated before, the cranial somitomeres, which are mesenchymal metameric units, continue to expand as the brain expands rather than condensing into somites. Somitomeres form a continuous sequence from the tip of the head to the tip of the tail. Some experiments suggest that cranial somitomeres may be able to form somites. When the cranial end of a chick embryo, a part that normally would form only cranial somitomeres, is explanted, a series of somites forms instead [28].

Cranial somitomeres are closely associated with specific regions of the forming brain. When brain parts expand a lot, the somitomeres associated with the brain part also expand. The amniotes expand their brains extensively, basal vertebrates less so.
Figs. 5 to 10 are drawings of cranial somitomeres from representatives of six classes of vertebrates. These drawings are from various published sources. Lamprey cranial segments (Fig. 5) come from the study by Damas [29] and are a reconstitution from cross-sections. An SEM study by Kuritani *et al.* [30] for a different species of lamprey produced essentially the same picture. A classic illustration by Goodrich [31] is the basis

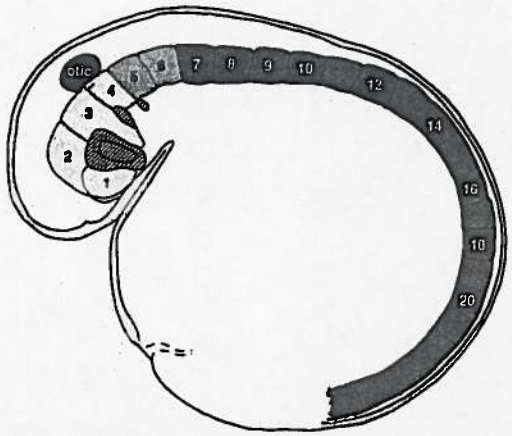

Fig. 5. Left lateral view of the mesodermal segments (shaded, numbered) of a lamprey embryo *(Lampetra fluviatilis)*. The head mesoderm by this stage is segmented and isolated from other tissues. There are four cranial mesodermal segments. The otic placode lies over the fourth somitomere. Pharyngeal pouches are in white. Other tissues are not indicated in this modified drawing to emphasize the mesodermal segments. The first mesodermal head segment is the premandibular, the second the mandibular, the third the hyoid. (Modified from Damas [29], his reconstitution Fig. 5, embryo of 21 segments.

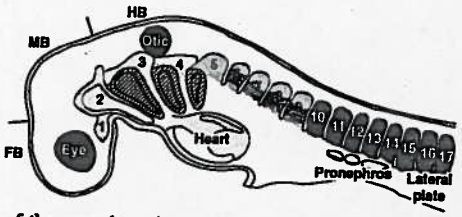

Fig. 6. Left lateral view of the mesodermal segments (shaded, numbered) of a shark embryo *(Scyllium canicula)* ; 5 mm long. There are four cranial mesodermal segments. The first three gill slits are in white. The trunk begins just anterior to the pronephric rudiment. Brain parts are closely related to somitomere positions; somitomere one with forebrain (FB), two with midbrain (MB), and three to about nine or ten with the hindbrain (HB). This drawing is from Goodrich [31], his Fig. 237, and modified to emphasize the mesodermal segments.

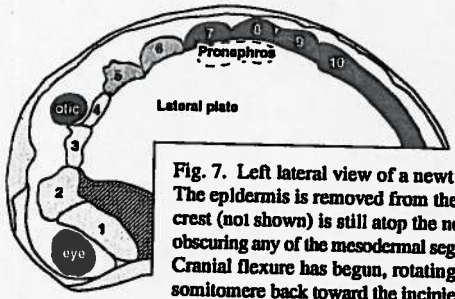

Fig. 7. Left lateral view of a newt embryo *(Taricha torosa)*. The epidermis is removed from the left side, and the neural crest (not shown) is still atop the neural tube and not yet obscuring any of the mesodermal segments (shaded, numbered). Cranial flexure has begun, rotating the first (premandibular) somitomere back toward the incipient hyomandibular groove. Segments one to four are the cranial somitomeres. The occipital somites are segments five and six. Segment seven is the first cervical somite, and it overlies the rostral end of the forming pronephric bulge. Lateral plate mesoderm lies beneath somitomere three (hyoid somitomere) and all somitomeres and somites posterior to segment three, but somitomeres one and two always lack lateral plate. This drawing is traced from an SEM in Jacobson and Meier [19], their Fig. 2, of a stage 23 embryo.

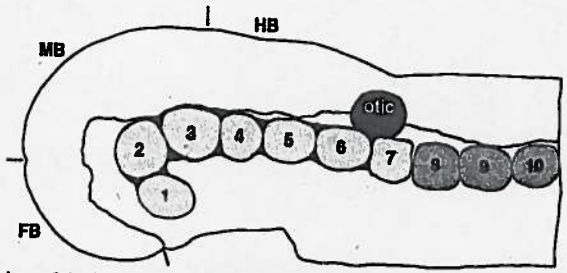

Fig. 8. Dorsolateral view of the left paraxial mesoderm of a snapping turtle embryo *(Chelydra serpentina)*. The ectoderm has been removed. There are seven cranial somitomeres (numbered 1-7). Three (8-10) of the four occipital somites are shown. The otic placode resides above and between the sixth and seventh somitomeres. The first somitomere is associated with forebrain (FB), the second and third with mesomeres of the midbrain (MB), the 4th to 7th and occipital somites 8-11 are associated with hindbrain (HB). This drawing is modified from an SEM illustration in Meier and Packard [32], their Fig. 10.

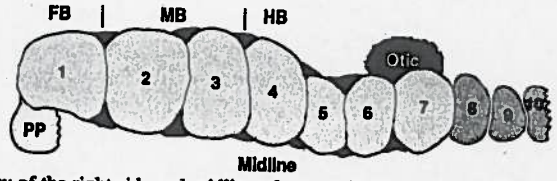

Fig. 9. Dorsal view of the right side and midline of a stage 8 chick embryo. The neural and non-neural ectoderm and the notochord were removed. The segments of paraxial mesoderm (somitomeres and somites) are numbered. The cranial segments (numbers 1-7) are somitomeres that will continue to expand. Segments 8-11 are occipital somites. PP = prechordal plate; FB = forebrain; MB = midbrain; HB = hindbrain. This diagram is modified from an SEM illustration in Meier [2] his Fig. 8.

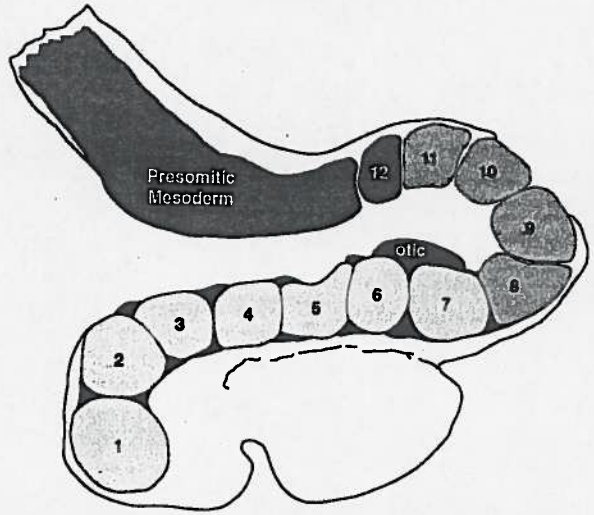

Fig. 10. Dorsomedial view of the right half of a mouse embryo from which the neural plate has been removed. The cranial somitomeres are numbered one through seven. These somitomeres are followed by five formed somites, the four occipital somites (8-11) and the first cervical somite (12). The somitomeres composing the rest of the paraxial mesoderm are in the presomitic mesoderm (unnumbered). The head somitomeres and somites are associated with brain parts as in the turtle and chick. This drawing is modified from an SEM illustration in Meier and Tam [33], their Fig. 21.

for a shark representative (Fig. 6). A study by Jacobson and Meier [18] is the example for an amphibian (newt) (Fig. 7). These taxa have a common number of four cranial somitomeres. In each case, the otic placode or vesicle lies between and over somitomeres three and four. The first somitomere is adjacent to the forebrain, the second to the midbrain, and the third, fourth and the occipital segments to the hindbrain.

Drawings from three SEM studies illustrate cranial somitomeres in amniote embryos: a reptile (turtle) (Fig. 8) from Meier and Packard [32], a bird (chick) (Fig. 9) from Meier [2] and a mammal (mouse) (Fig. 10) from Meier and Tam [33]. Each of these taxa have a common number of seven cranial somitomeres with the otic vesicle residing between the above somitomeres six and seven. In the heads of these amniotes, besides the seven cranial somites, are four occipital somites (segments 8 to 11).

Amniote embryos have doubled the numbers of somitomeres, except for number one (the premandibular segment) which remains associated with the entire forebrain. Somitomeres two and three are adjacent to the midbrain. The remaining head segments (4 to 11) lie next to the hindbrain. A similar number and distribution of head somitomeres was found in a teleost embryo (*Oryzias latipes*) [34].

Brains of amniotes enlarge early and rapidly. In the chick embryo, rapid brain enlargement begins near the end of the second day of incubation at stage 12. The total volume of the brain anterior to the rostral border of the first rhombomere of a chick embryo increased by 29-fold between days 3 and 5 (from stage 18 to 26) [35]. Amniotes may have adapted to rapid brain enlargement partly by nearly doubling the numbers of somitomeres in their heads.

Cranial somitomeres are associated with specific brain parts and even though they do not condense into somites, somitomeres could influence the positioning of cranial nerves. One would expect the cranial nerves to attach to the brain adjacent to the regions of the anterior parts of somitomeres as spinal nerves do adjacent to the anterior compartments of somites. They appear to do so and these relationships have been discussed before [3-6].

Somitomeres have so far been described in eight species in six vertebrate classes [6]. When Stephen Meier died, he had begun a study of somitomeres in another species, the whiptail lizard (*Cnemidophorus uniparens*). Fig. 11 shows some trunk somitomeres of this lizard in an SEM from the files of Meier.

6. Some Contrary Views of Somitomeres

Some published accounts question the existence of, or the relevance of, somitomeres. Stern and Keynes [36] make the assumption that a metameric pattern of somitomeres requires that there be little or no cell movement within the segmental plate, or at least that any movement be restricted to within somitomeres. They say, based upon unpublished observations, that this is not the case.

Being mesenchymal cells, the cells of somitomeres naturally move about. This is a general characteristic of vertebrate embryonic tissues, including even cells in epithelial tissues such as the neural plate and tube in which changing of neighbours of cells is extensive [37]. Mesenchymal cells of the limb bud move about, but no one denies their leg.

The presomitic mesoderm is a morphologically patterned field of somitomeres which are prospective somites. It should be expected that regulation would occur in such a patterned field. When chick segmental plate is cut into bits and the fragments are mixed [38,39], the pattern of somites that emerges is normal. Also, extirpation of future intersomitic furrows from chick segmental plates did not prevent normal somite pattern [40].

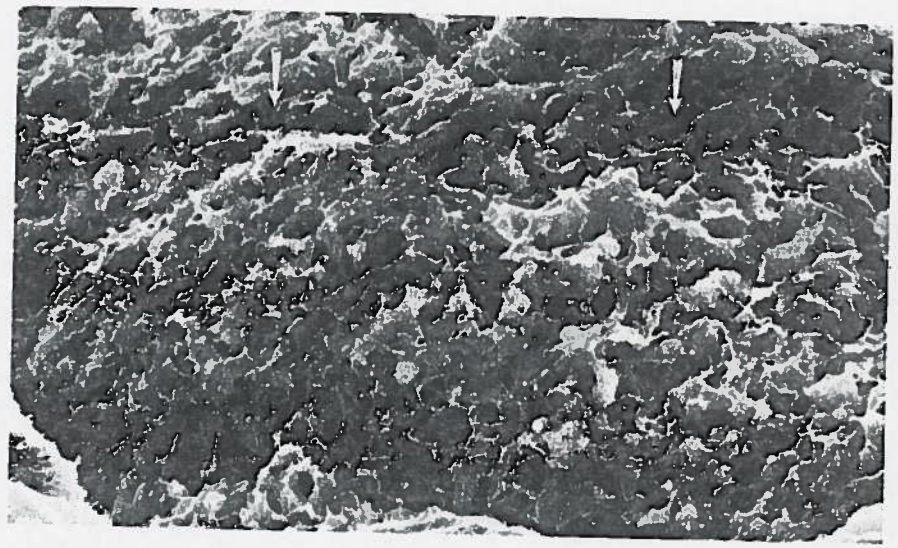

Fig. 11. Scanning electron micrograph of a dorsal view of two somitomeres in the segmental plate of an embryo of the whiptail lizard, *Cnemidophorus uniparens*. Arrows indicate the midpoints of the rostrocaudal axis of each circular somitomere. (From S.P. Meier, unpublished).

Many patterned mesenchymal groupings emerge within fields of other mesenchymal cells. Such patterns likely arise as groups of cells sort out from the surrounding cells by acquiring differences in cell surface adhesion molecules. As mentioned above, the somitomeres in the segmental plate are in the process of becoming epithelialised so their cell-surface characteristics likely differ one somitomere to another. Also, the emerging evidence from molecular expression patterns indicates that the segmental plate already has at least a labile somite pattern as we noted above, and that pattern is the pattern of somitomeres. Half-segments are also in the process of being determined.

The intersegmental blood vessels that form at the boundaries between all the somitomeres in the segmental plate of the chick embryo have recognised those prospective somite boundaries.

It is claimed that somitomeres exchange cells, but the evidence is not conclusive. For example, one study [41] labelled paraxial mesenchymal cells in culture with wheat germ agglutinin-gold conjugate and grafted (injected) them orthotopically into the anterior, middle or posterior regions of the presomitic mesoderm of mouse embryos at the four to seven somite stage. Labelled cells colonised somites that formed from the region into which they were injected and also from more posterior regions. The study concluded that there is a general posterior movement of cells in the presomitic mesoderm of the mouse and that there must be considerable cell mixing among somitomeres in the presomitic mesoderm.

I disagree that these experiments demonstrate that mixing of cells normally occurs among somitomeres. Injected cells came from similar regions of the presomitic mesoderm into which they were injected, but the cell surface characteristics of the labelled cells were undoubtedly changed considerably by the culturing and labelling process and they could

be expected to sort out in possibly unusual ways. The more posterior they are injected, the more mesenchymal and less epithelial the resident cells would be and the more extensively might the injected cells sort out. Furthermore, many injected cells may initially have come to occupy the crotches between somitomeres and what becomes of those cells is not known for sure, but it is likely they are, or contribute to, the vascular endothelial cell population that moves around contributing to blood vessels.

In any event, the contention that metameric patterns must have compartment properties is a gratuitous assumption. Morphology is often ahead of final patterning in embryos. We must remember that vertebrate embryos may regulate even rather late in development, such as the well-known case of the eye-forebrain field of a salamander persisting as late as the optic vesicle stage so an explanted optic vesicle will still form an eye and a forebrain. Somitomeres are metameric morphological units that form somites even if they pass around a few cells.

Some people claim that cranial somitomeres do not exist. For example, Jacob *et al.* [42] reported a computer assisted study of densities of nuclei (thus cell densities) in somites and cranial somitomeres. They concluded "that a metameric pattern does not exist rostral to the first somite" (their Page 85). Since all somitomeres begin as expansion figures, and the pre- and subotic somitomeres continue to expand along with the brain rather than condense as somites do, this study is a *non sequitur*; based on a false premise. Furthermore, somitomeres 1 and 2 are quite clearly shown in the scanning electron micrograph of their Fig. 7, the legend for which says "A metameric pattern is not recognisable in the paraxial mesoderm".

A similar, though somewhat more extensive, study was published in 1996 by Freund *et al.* [43], entitled "The metameric pattern of the head: does it exist?" They conclude it does not, but their study is based on the same false premise as the one just mentioned, and thus is another *non sequitur*.

Some published criticisms of somitomeres are rather brief. For example, cranial somitomeres are dismissed in half of a sentence by Lumsden and Keynes [44]. They say "In contrast to the trunk, paraxial mesoderm segmentation in the head is inconsequential, ...". An unsupported opinion like that is of no consequence. The relationships between cranial somitomeres and rhombomeres is referred to in Section 5 above. It remains likely that the cranial somitomeres influence the segmentation of the hindbrain and the positions of the cranial nerves.

7. Some Evolutionary Considerations

When one considers and compares the ontogeny and phylogeny of chordates, it appears that segmented units of paraxial mesoderm (somitomeres and somites) have two origins. As noted above, there are separate induction systems for head and tail. Induction of the dorsal mesoderm by Nieuwkoop's centers in the endoderm is similar among the chordates [45].

The head mesoderm (future prechordal plate and some cranial somitomeres) is induced by head signals and is the first mesenchyme to begin migrating to its final position at commencement of gastrulation in amphibian embryos. The trunk segments and those in the head up to the second segment become strung out in the rostral direction by anteriorly-directed convergence and extension movements of the notochordal and other cells during gastrulation. All these segments, to varying degrees, are likely induced in the pregastrula and gastrula stages by overlapping head and tail signals. Prospective tail paraxial mesoderm, induced entirely by tail signals in the pregastrula, is left at the

blastopore lip at the end of gastrulation and is extended caudally by posteriorly-directed convergence and extension movements of the cells during later stages.

The phylogeny of segments also may be reflected in the ontogeny of mesodermal segments of the chick embryo. The most-cranial somitomeres (the premandibular and the mandibular segments) are formed during formation and elongation of the prospective primitive streak [15]; the remaining segments are formed sequentially during primitive streak regression and at first appearance are positioned just posterior to each side of Hensen's node in Spratt's "somite forming centers".

One of our relatives, the tadpole of the ascidian larva, has a functional tail which is more or less segmented and is extended by posteriorly-directed convergence and extension movements of the cells of the notochord and paraxial mesoderm. The tadpole also has a head with mesodermal components, but the head has only partial development in most forms which have transient tadpoles.

The craniates, like the tunicates, may have evolved from fossil forms, the mitrates [46,47]. An adult mitrate had just a head and a tail. The tail was segmented and had a notochord. The head contained two pairs of mesodermal segments, the premandibular and the mandibular segments. The ascidian tadpole is in many ways similar to the mitrate form. The craniate form, with a new trunk and posterior head, likely evolved from the mitrate form by overlapping of the head and tail fields during the signaling period of the pregastrula stage [48].

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