The Development of Radial and Biradial Symmetry:  
The Evolution of Bilaterality

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SYNOPSIS. Understanding the evolutionary origin of novel metazoan body plans  
continues to be one of the most sought after answers in biology. Perhaps the most  
profound change that may have occurred in the Metazoa is the appearance of  
bilaterally symmetrical forms from a presumably radially symmetrical ancestor.  
The symmetry properties of bilaterally symmetrical larval and adult metazoans  
are generally set up during the cleavage period while most “radially” symmetrical  
 cnidarians do not display a stereotyped cleavage program. Ctenophores display  
biradial symmetry and may represent one intermediate form in the transition to  
bilateral symmetry. The early development of cnidarians and ctenophores is com-  
pared with respect to the timing and mechanisms of axial determination. The origin  
of the dorsal-ventral axis, and indeed the relationships of the major longitudinal  
axes, in cnidarians, ctenophores, and bilaterian animals are far from certain. The  
realization that many of the molecular mechanisms of axial determination are  
conserved throughout the Bilateria allows one to formulate a set of predictions as  
to their possible role in the origins of bilaterian ancestors.

INTRODUCTION

Recent reports indicate that there is surprising conservation in the cellular and mo-  
lecular basis of embryonic patterning events in organisms as diverse as mice and  
insects. One can only wonder how deeply rooted these mechanisms are within the  
Metazoa, and how such a diverse array of creatures could have evolved from an an-  
cestor that utilized these conserved patterning mechanisms. Bilaterally symmetrical  
organisms, the Bilateria, are likely to have evolved from some kind of ancestor with  
a cnidarian- or ctenophore-like level of body construction, as members of the so-called  
“Radiata” (Morris, 1993; Wainright et al., 1993; Brusca and Brusca, 1990). When at-  
tempting to formulate theories about how such a radical change in the body plan  
could arise, one must have some under-  
standing of the developmental basis for  

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their construction. In contrast to many bi-  
laterians, we know little about the develop-  
ment and evolution of members of the Radiata. The evolution of the Bilateria, by  
definition, is ultimately concerned with the origins of the dorsal-ventral and bilateral  
axes, yet little information is currently available to suggest how these major body  
axes might have evolved. This paper re-  
views various aspects of axial specification  
in the Radiata, including some of recent  
work on ctenophore embryos, and address-  
es issues regarding the invention of stere-  
otypical cleavage programs and the possible  
transitions between radial, biradial and bi- 
laterally symmetrical body plans.

THE RADIATA

The two eumetazoan phyla which com-  
prise the Radiata are the cnidarians and the  
ctenophores. The major adult body axis of  
both ctenophores and cnidarians is the  
“oral-aboral” axis. In both phyla, the outer  
eridinal epithelium surrounds an inner  
gastrodermic pouch that opens at the mouth  
(Fig. 1). Separating these two layers is the  
mesoglea, a largely acellular extracellular  
matrix. Although individual cells reside
FIG. 1. The normal body plan of the two phyla of the “Radiata,” cnidarians (A, B) and ctenophores (C, D). Both phyla are “diploblastic” and possess an outer epidermis and inner gastrodermis (darkly shaded) separated by a largely acellular mesoglea. The cnidarians generally have multiple planes of mirror symmetry which pass through the major longitudinal axis, the oral-aboral axis. A. Cross section of the benthic polyp form which attaches to the substrate via the basal discs located at the aboral pole. Numerous tentacles surround the mouth. B. Cross section of the pelagic medusa morph. These animals swim with their mouths trailing behind. C. Lateral view of a tentaculate stage ctenophore (e.g., Mnemiopsis) with the aboral pole located towards the top of the page. Note that the apical organ is located on the aboral surface and is connected to each ctene row via a ciliated groove. These animals are approximately 0.5 mm in diameter after hatching from their vitelline membrane and retain this morphology until they are approximately 4.0 mm when they transform into lobate stage adults (not shown). D. Diagrammatic representation of the tentaculate stage ctenophore as seen from the aboral pole. There are eight ctene rows located on the surface of the animal and two tentacles used for capturing prey. The endodermal canals open centrally to the stomach and terminally they run subjacent to each of the ctene rows. Ctenophores were previously considered as “biradially symmetrical” with planes of symmetry passing through the tentacle sheathes, and esophageal plane. (The two polar fields associated with the apical organ run along the esophageal plane.) We now recognize, however that there are no true planes of mirror symmetry; rather, there are an infinite number of planes of rotational symmetry due to the oblique placement of the two anal canals. Thus, any two “halves” of a ctenophore bisected along the oral-aboral axis are only superimposable when one is rotated 180 degrees around the oral-aboral axis.
within or wander through the mesoglea, no true mesodermal tissue layer is present, and hence these organisms are often referred to as "diploblastic." While the gastric cavity is blind in cnidarians, ctenophores possess two small openings on either side of the apical organ, the anal pores, which connect the gut cavity to the outside environment. Effectively, the mouth also acts as an anus, since the anal pores are too small to pass the majority of undigested matter.

Due to the complex and diverse life history strategies present in the Cnidaria, distinctly different benthic and pelagic forms are often generated. Most cnidarians display variations of one or both of the following morphs: a sessile polyp with a mouth surrounded by tentacles located at the oral end of the longitudinal axis and a basal disc or holdfast located at the aboral end (Fig. 1A). Alternatively, a free-living pelagic medusa may be formed that possesses its mouth at the tip of the manubrium, which is suspended beneath a swimming bell (Fig. 1B). In most cnidarians, embryogenesis results in a solid ciliated planula larva (with no mouth or functional gut) that has only a single recognizable, anterior-posterior, axis. The planula eventually metamorphoses into a sessile polyp in which the anterior pole (defined by swimming direction) becomes the basal disc (holdfast) and the posterior pole becomes the mouth. In hydrozoans, the polyp later buds a pelagic medusa which will go on to form functional gametes. In anthozoans, the polyp morph produces gametes directly. On the other hand, virtually all ctenophores are pelagic animals with direct development. There is no true larval phase and embryogenesis results in the production of a cydippid stage adult. In some orders, the cydippid undergoes additional growth that transforms it into a secondarily-derived adult, but this does not entail a radical metamorphosis or change in the basic body plan.

Of special interest is the diverse variation in symmetry seen in members of the Radiata. Both cnidarians and ctenophores now show various forms of symmetry in planes passing along the oral-aboral axis (Fig. 1). In some cnidarians, this takes the form of multiple planes of mirror symmetry, hence the moniker "radial symmetry". There is morphological evidence in some cnidarians that the number of planes of symmetry may be reduced, and that biradial (with two major planes of symmetry) or even bilateral body plans are present (with only one plane of mirror symmetry). For example, some hydrozoan medusae have scores of tentacles surrounding the margins of the bell, while other species have only two or four tentacles. Most adult anthozoans (e.g., corals and sea anemones) possess indicators of bilateral symmetry in the folded pleats of their gastrodermis. Recent evidence indicates that anthozoans are the basal members of the Cnidaria (Bridge et al., 1995; Odorico and Miller, 1997) and so it is possible that ancestral cnidarians were not radially symmetrical.

The symmetry properties displayed by ctenophores are significantly different from those of cnidarians and may represent an intermediate step in the evolution of bilaterality. Ctenophores have been described as being biradially symmetrical, with two perpendicular planes of symmetry (Fig. 1D) that run through the two tentacles (the tentacular plane) and the plane of the flattened esophagus (the "sagittal" plane) that define four body quadrants. The endodermally derived anal canals connect the gut to the external environment via the anal pores which are located at the aboral surface in two diametrically opposed quadrants (Fig. 1D). Thus, the tentacular and sagittal planes of symmetry are not simple planes of mirror symmetry. Instead, these represent planes of two-fold mirror (rotational) symmetry. Thus, any plane that includes the oral-aboral axis represents a plane of rotational symmetry, including both the plane that passes through the anal pores and the plane orthogonal to it. In fact, ctenophores do not possess a single true plane of mirror symmetry. The diverse nature of symmetry properties amongst members of the Radiata raises several questions. Do their symmetry properties bear some relationship to those of bilaterians? Does the establishment of rotational symmetry have a different developmental/molecular basis than the establishment of mirror symmetry? For instance, the presence of diametrically distinct quad-
rants in ctenophores, which eliminates true radial symmetry, may represent precursors of secondary polarized axes, such as the dorsal-ventral axis of bilaterians. On the other hand, radial symmetry may represent a derived condition, and all eumetazoans may actually be constructed upon an underlying bilaterally symmetrical platform.

An understanding of the developmental basis of the symmetry properties in the Radiata is needed before any relationship to the evolution of bilaterian body plans can be obtained. This information will be difficult to interpret, however, since the phylogenetic relationships of these phyla to bilaterians, and to each other, have not yet been clarified. While cnidarians and ctenophores appear to occupy pivotal positions in metazoan phylogeny, there is no consensus as to their exact relationships to other extant phyla. Historically, ctenophores have been grouped with cnidarians as the Coelenterata (Christen et al., 1991; Morris, 1993) and compelling arguments have also been proposed which would either make the cnidarians the sister group to the bilaterians (Wainright et al., 1993) or position ctenophores as degenerate deuterostomes (Nielson, 1995). On the basis of developmental and morphological evidence, and for the sake of argument, we currently favor the view (Fig. 2) that ctenophores are the sister group to the Bilateria (Harbison, 1985; Ax, 1989; Schram, 1991; Eernisse et al., 1992). However, the next few years should bring us to a better understanding of early metazoan phylogeny.

**EARLY DEVELOPMENT AND AXIAL SPECIFICATION IN THE RADIATA**

What little is known about the relationship of early development to the formation of the body axis in cnidarians is derived from a handful of different hydrozoan species (Tessier, 1931; Freeman, 1980, 1981, 1983, 1990). These studies have pointed out significant parallels with some aspects of development in ctenophores (Freeman, 1983). The eggs of both cnidarians and ctenophores are centrolecithal and possess a thin peripheral layer of cytoplasm surrounding a central yolk mass. Experiments have shown that fertilized eggs of both hydrozoans and ctenophores lack any meaningful axial information that is used to construct the embryo, including the animal-vegetal axis. Rather, the major longitudinal body axis is normally set up by the initiation site of the unipolar first cleavage division. These features tend to unite

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**Fig. 2.** Diagram indicating one likely relationship between "radially" and bilaterally symmetrical metazoans. Recent work suggests that the ancestral bilaterians displayed radial, indeterminate cleavage and enterocoely. Several key features of early development are mapped onto this presumed phylogeny. (Valentine, 1997; Goldstein and Freeman, 3; Martindale and Henry, 1997b; Martindale and Henry, 1995; in preparation.)
the ctenophores and cnidarians because no other metazoans appear to display these developmental features (Goldstein and Freeman, 1997). It is interesting to note, however, that the oral pole of adult cnidarians (hydrozoans) is generated from the posterior pole of the planula larva. This seems to indicate that there is an “inversion” of axial properties in cnidarians between different life history phases and that the relationship of the earliest determinative events are conserved relative to the adult body plans in these two taxa.

In most metazoans, a stereotypical species- and often phylum-specific cleavage program ensues after fertilization. Virtually all cnidarians lack such a regular cleavage program. In fact, cnidarian development often involves “chaotic” cleavage in which no two embryos in the same spawning will exhibit an identical cleavage pattern. In some species, cleavage furrows regress, forming temporary syncytia that cellularize at later stages of development. The absence of a cleavage program suggests that cells do not become reproducibly positioned with respect to other cells and that it is impossible to identify homologous cells from embryo to embryo. In contrast to cnidarian development, ctenophores develop according to a highly stereotypic and phylogenetically unique cleavage program not shared by any other extant phylum. For example, each of the first four cell divisions in ctenophores is associated with important developmental decisions. First cleavage establishes the oral pole and sagittal axis (Freeman, 1977). Second cleavage establishes the tentacular and anal axes (delimits the “/” vs. “\” quadrants, Fig. 3; see Martindale and Henry, 1995; in preparation). Third cleavage delineates the E and M lineages and involves the differential segregation of light producing potential to the M cells, and comb plate potential to the aboral pole (Freeman and Reynolds, 1973). Fourth cleavage segregates the comb plate-forming potential to the e, (Reverberi and Ortolani, 1963; Farfaglio, 1963) and m, micromeres and comb plate-inducing potential to the e, micromeres (Martindale and Henry, 1997b). These determinative events in the early cleavage program are accompanied by the condition in which ctenophore embryos have virtually no capacity to regulate following the removal of various embryonic regions (Chun, 1880; Martindale and Henry, 1997b). In most cnidarians, however, there is no evidence of regional specialization other than the initial formation of the oral pole at first cleavage. Subsequent cleavages are not utilized to establish pattern along or around the major longitudinal body axis, and no differences can
be identified amongst the embryonic cells (Freeman, 1983). Instead, cells appear to become determined at later developmental stages by virtue of cell-cell interactions that operate within developmental fields (Freeman, 1981). Thus, the timing of cell commitments and the ability to regulate are dramatically different between members of the Radiata.

This is not to say that in ctenophores each and every cell is determined at the time of its birth. Recent work has shown that cell-cell interactions are required for the normal appearance of comb plates by micromere descendants and the endodermal canals in ctenophore embryos (Martindale, 1986; Martindale and Henry, 1997). The cleavage process is involved in segregating the developmental potential for this inducing activity to the micromere lineages. The lineage-specific signaling activity observed in ctenophores and in virtually all bilaterians illustrates another, often overlooked, aspect of stereotypical cleavage programs, namely that cells are generated and reside in predictable locations within the embryo. Stereotyped cleavage programs can not only segregate inducing potential to discreet regions of the embryo, but also place other cells in defined and reproducible locations with respect to these signaling centers. The fact that individual cells assume reproducible fates within the ctenophore embryo has led to the false assumption that all identified cell lineages are defined precociously (Reverberi, 1971; Ortolani, 1989). Only experimental intervention is able to discriminate between cells that are specified early, and those whose determination requires interactions with adjacent cells. The most dramatic example of this phenomenon is seen in the development of the soil nematode C. elegans in which numerous cell interactions play an important role during early embryogenesis despite the occurrence of stereotyped cleavage patterns (see Schnabel, 1997 for a recent review).

The notion that stereotypical cleavage programs were co-opted early in metazoon evolution to localize developmental potential is reinforced by the finding that there are some highly derived cnidarian embryos that display rudimentarily discrete cleavage programs. Experiments by Freeman (1983) have also shown that some trachyline hydrozoans and the bilaterally symmetrical siphonophores also segregate developmental potential via the early cleavage divisions. In one, but not all species of siphonophore, first cleavage corresponds to the sagittal body axis. In other species, the fates are associated with the appearance of distinct germ layers at the eight-cell stage, separating prospective endoderm from ectoderm. While these determinative decisions are not obviously homologous to the cell lineage decisions taking place in ctenophores they indicate that regular cleavage programs in basal metazoans can be recruited to accomplish different developmental decisions. Does the co-option of stereotypical cleavage patterns, which segregate developmental potential within an isotropic egg, represent an important step in the generation of novel body plans (e.g., conversion between radial, biradial or bilateral symmetry)? If cnidarians and/or ctenophores are derived from bilaterally symmetrical forms then the variations in cleavage programs and timing of cell commitment events might have more to do with changes in life history strategy than with changes in body plan. For example, ctenophores, siphonophores and trachyline hydrozoans are all direct developers and the precocious segregation of developmental potential may be related to the advantages in the rapid formation of the adult body plan (Freeman, 1981, 1983).

The precocious segregation of developmental potential present in ctenophore embryos is not shared by all metazoans. One of the primary roles of the cleavage program in metazoan evolution might have been to establish “signaling centers” which helped direct the fates of neighboring cells. In that they lack a stereotyped cleavage program, cnidarians do not appear to possess this capacity, and every cell is functionally interchangeable with any other cell during the early phases of development. Virtually all other metazoans demonstrate localized sites or “poles” of inductive activity. For example, several metazoan phyla display a pattern of cleavage known as spiral cleavage. In these forms, the dorsal-ventral axis
is "organized" by the so-called D quadrant. The early spiralian cleavage program is extremely important in both the establishment of the D quadrant, as well as the organizing influence the D quadrant macromere has on adjacent cells (See Verdonk and Cather, 1983; van den Biggelaar and Guerrier, 1983; see also the paper by Boyer and Henry, 1998). In some situations such signaling centers have profound global effects on axial organization (e.g., vertebrate, echinoderm, nematode, and spiralian phyla) while in others they may serve to provide localized inductive cues (ctenophores). This strategy is in marked contrast to the evolution of a complex cleavage program in which fates of each and every cell are predetermined during the embryonic period as a "mosaic" of individual parts of the larval or adult body plan. It should be noted that no organism exhibiting such a "mosaic" pattern of development has ever been found. Recent arguments have been made that bilaterian ancestors displayed radial and indeterminate cleavage (Valentine, 1997). Figure 2 indicates some of the key features of early embryogenesis at the base of the Metazoa. The role of the cleavage process and regional determination in metazoan evolution has been thoroughly covered elsewhere (Davidson, 1991).

**RELATIONSHIP OF AXIAL PROPERTIES IN THE RADIATA AND BILATERIA**

A variety of possible scenarios for early evolution in the Metazoa have been considered in detail (Hyman, 1940; Hadzi, 1963; Salvini-Plawen, 1978; Neilsen, 1995). If bilaterians are derived from a radially or bi-radially symmetrical stock, how did these new symmetry properties arise? Did the evolution of a new axis, the dorsal-ventral axis, arise from an already existing axis, like the tentacular or anal axes? Or, did it arise de novo? Bilaterality might have appeared by a suppression or modification of aspects of a radially symmetrical patterning mechanism in which only a single axis was co-opted for future elaboration. Recently discovered fossils from the Mid- and possibly even Lower-Cambrian (Morris and Collins, 1996) suggest that ctenophores may have once had as many as 80 comb rows and that there has been a reduction to the stable 8 rows present in all extant comb-bearing species. Does this reduction in morphological complexity represent a move to bilaterality within the Radiata? In other words, do such axes as the dorsal-ventral axis arise de novo in a polarized fashion via the establishment of a localized signalling center, or do such axial properties arise from unpolarized axes that subsequently become polarized (like the anal axis of ctenophores)?

Ctenophores are composed of four nearly identical quadrants separated by the tentacular and esophageal (sagittal) planes (Fig. 2D). Each of these planes would define planes of mirror symmetry were it not for the presence of the anal canals. Cell lineage studies have shown that each of the four quadrants normally contributes to structures along both the tentacular and esophageal axes. For example, each of the first four cells gives rise to portions of one of the tentacular apparati. This situation is not true for the formation of the anal canals. Cell lineage analysis in the lobate ctenophore *Mnemiopsis leidyi* has revealed a phenomenon that we refer to as "diagonal determination" (Martindale and Henry, 1995). The two endodermally-derived anal canals are generated from descendents of diagonally opposed 2M macromeres at the 60 cell-stage (the backslash or "\" pair). The other two 2M macromeres (the slash or "/" pair) do not contribute to the formation of anal canals, but they do make circumeosphageal and longitudinal muscle cells, which are not produced by the "\" lineages. Thus, these four seemingly identical 2M macromeres, which are all in contact with one another at the animal (oral) pole, are differentially organized as two pairs of diagonally opposed cells (Fig. 3). In fact, these quadrant specific differences are established at the four-cell stage.

Depending on whether radial or bilateral symmetry is ancestral, the anal axis of ctenophores could represent an incipient precursor, or a remnant, of the dorsal-ventral axis found in bilaterians. Does the formation of the anal axis in ctenophores tell us anything about how bilateral symmetry arose in metazoan evolution? Our ability to
FIG. 4. Diagram indicating some possible expression patterns of Hox genes in the Ctenophora. Predicted relationship of two Hox genes, including: an "anterior" Hox gene Cteno labial like and a “midbody” Cteno-Antp-like ortholog. (A) If “anterior” Hox genes are expressed around the oral pole one can argue that the common ancestor of protostomes and deuterostomes did not form mouths independently from a blind digestive tract, and this suggests that there was a shift of the mouth to the dorsal side in deuterostomes from an ancestral ventral location in protostomes (Lucalli, 1996). (B) If “anterior” Hox genes are expressed at the aboral end of ctenophores, one can argue that the oral pole of radially/biradially symmetrical organisms has become the anus of bilaterians, and that new mouths appeared independently in protostomes and deuterostomes. (C) Hox gene expression patterns may exhibit other relationships to the oral-aboral axis.

obtain answers to these questions is hampered by the fact that we do yet not understand the relationships of the major body axes of the Radiata to those of the bilaterians. It is often assumed that the major longitudinal axis of the Radiata (oral-aboral axis) is homologous to the anterior-posterior axis of bilaterians. However, there is no compelling evidence to support this claim, and even if it holds, it remains unclear which end of the oral-aboral axis corresponds to the anterior pole in bilaterians. This question has become all the more interesting and tractable due to recent work showing a conserved molecular basis for the formation of both the anterior-posterior and dorsal-ventral axes in bilaterians.

Several interesting implications arise when one considers the possible evolutionary transitions between radial and bilateral symmetry. Highly conserved and robust molecular markers currently exist for both the anterior-posterior (Slack et al., 1993; Akam, 1995) and dorsal-ventral axes (Ferguson, 1996; DeRobertis and Sasai, 1996) in all bilaterians thus examined, and it is likely that these genes are also expressed in radially and biradially symmetrical metazoans. The markers for the anterior-posterior axis are the Hox genes. Hox genes have been reported in both cnidarians (Schierwater et al., 1991; Schummer et al., 1992; Naito et al., 1993; Shenk et al., 1993a, b. Finnerty and Martindale, 1997) and ctenophores (Finnerty et al., 1996); however their patterns of expression have yet to be thoroughly explored in either group. A comparison of Hox gene expression in the Radiata might reveal the actual relationship of the longitudinal axes in these two groups. For example, if “anterior” Hox genes (such as a labial ortholog) are expressed closer to the mouth than “midbody” or “posterior” Hox genes, it would provide evidence that not only are the oral-aboral axis and the anterior-posterior axis homologous, but that the polarity along these axes has been conserved (Fig. 4A). The fact that adult ctenophores swim with their mouth forward, they possess anal canals on the side opposite the mouth, and the oral pole is derived from the “animal” pole of the embryo (as defined by the first cleavage division) suggests that the oral pole in ctenophores corresponds to the anterior pole of bilaterian descendants.

If, on the other hand, the polarity of Hox gene expression is reversed, and “anterior” genes are expressed closer to the aboral sense organ (Fig. 4B), it would suggest that the mouth of radially/bilaterally symmetrical metazoans is homologous to the anus of bilaterians and that the mouth may have evolved in different locations in protostome and deuterostome lineages (see below). Of course, it is also possible that the anterior-
FIG. 5. Possible scenarios for the formation of the metazoan dorsal-ventral axis and its implications for the relationship of the oral-aboral axis of radial/bilaterally symmetrical animals to the anterior-posterior axis of bilaterians. *dpp/BMP-4* and *sog/chordin* orthologs are likely to be involved in establishing the dorsal-ventral axis in both extant protostomes and deuterostomes (see Ferguson, 1996 for review). The position of the neurogenic region of both protostomes ("ventral") and deuterostomes ("dorsal") is marked by the expression of *sog/chordin* orthologs (shading). A. Formation of a deuterostome body plan from a protostome-like ancestor that already possessed well-defined anterior-posterior and dorsal-ventral polarity. The position of the mouth changed in deuterostomes such that the mouth forms on the side opposite the central nervous system. B. The mouth of protostomes and deuterostomes could have formed independently from an ancestor that possessed a
posterior axis is not homologous with the oral-aboral axis. It could be, for example, that the oral-aboral axis corresponds more closely with the dorsal-ventral axis (Fig. 4C). For example, there are some derived ctenophores which have abandoned their pelagic existence and live on the sea floor. These "creeping" ctenophores lose their comb rows late in embryogenesis and move about with their mouth towards the substrate (i.e., "ventral") but with no preferred direction of movement, that is, no anterior-posterior polarity (G. Freeman, personal communication). In addition, it could be that the relationship of the oral-aboral axis is different between ctenophores and cnidarians, requiring that we completely re-evaluate the phylogenetic relationship of these organisms to other extant metazoans (see Nielsen, 1995, for example). Finally, Hox genes may not be deployed in axis specification, but may be involved in cell type determination or other developmental functions (Davidson, 1991).

Lacalli (1996) has pointed out two possible scenarios for the evolution of the dorsal-ventral axis in bilaterians that also have implications for the formation of the anterior-posterior axis. In one scenario, an ancestor possessed a continuous digestive tract and dorsal-ventral polarity (as evidenced by the placement of the central nervous system and mouth on the ventral side). Deuterostomes, which utilize orthologous genes to establish the dorsal-ventral axis (see below), would have evolved by the formation of a new mouth, or through migration of the existing mouth to the ancestral "dorsal" side of the embryo (Fig. 5A). This scenario is complicated by the difficulty of envisioning transitional forms where the mouth attains the new position. Another scenario predicts that the common ancestor of both protostomes and deuterostomes possessed a blind gut and a dorsal-ventral axis. In this case, mouths would have evolved independently on different sides of the embryo with respect to the dorsal-ventral axis in protostome and deuterostome lines (Lacalli, 1996). If this scenario is true, it implies that there might have been an "inversion" of the anterior-posterior axis, where the mouth (the common mouth and anus) of the ancestor became the anus of bilaterians (Fig. 5B). The possible "inversion" of the oral-aboral axis points to the uncertainty in the evolutionary relationship of the body plans of radially and biradially symmetrical organisms to those of bilaterians. No good transitional organism extant, or fossilized, has yet been identified and the number of potential candidates, including the flatworms, appears to dwindle as the phylogenetic relationships of the Metazoa are unraveled (Aguinaldo et al., 1997; Ballavoine, 1997; Valentine, 1997).

A third scenario can also be considered (Fig. 5C). If a ctenophore-like organism represents the ancestor of both protostomes and deuterostomes, their descendants might have co-opted an existing axis (such as the anal axis) for constructing the dorsal-ventral axis. In this situation, asymmetric polarity along that axis would develop, possibly as the ancestors assumed a benthic existence, and descendant lines would have had to utilize one of the anal canals as their new mouth. Whether the anal pores of ctenophores represent the sites of either the protostome or deuterostome mouth remains to be seen.

There should be a way to determine whether the ctenophore anal axis (or other axes such as the tentacular or esophageal axes) represents an incipient dorsal-ventral axis. Recently, two sets of genes have been identified in fly and amphibian embryos which are causally involved in the establishment of dorsal-ventral polarity. This ancestor was presumably derived from a radially symmetrical stock possessing no dorsal-ventral axis and a peripheral nerve net along the oral-aboral axis. C. Deuterostomes and protostomes could have been derived through the selective loss of one of the anal canals from a ctenophore-like ancestor. This suggests that the anal axis of ctenophores corresponds to the future bilaterian dorsal-ventral axis and that polarity along that axis evolved secondarily. A = anus, M = mouth. The ? indicates a possible pattern of expression for dorsal-ventral patterning genes. It is not yet known whether members of the Radiata possess dpp/BMP-4 or sog/chordin orthologs. See text for additional details. (A, and B, after Lacalli, 1996).
lishment of the dorsal-ventral axis. One of these pairs of orthologous genes, the fly sog (short of gastrulation) and an ortholog in amphibians, chordin, have been shown to be functionally interchangeable with one another (Ferguson, 1996; DeRobertis and Sasai, 1996). sog is expressed in the ventral region of fly embryos, while its ortholog, chordin, is expressed in the dorsal region of amphibian embryos. When chordin is injected into fly embryos it promotes ventral fates, and when a modified sog is injected into frog embryos it promotes dorsal fates. The situation is identical, but complimentary, for the two genes decapentapalegic (dpp) from flies and Bone Morphogenic Protein-4 (BMP-4) from frogs. While dpp is expressed in the dorsal regions of the fly embryo, BMP-4 is expressed in the ventral regions of frog embryos. The most parsimonious interpretation of these results is that there has been a functional conservation in the molecular basis for dorsal-ventral polarity in protostome and deuterostome evolution. Care must be taken in the analysis of this signalling pathway, however, since antagonistic biochemical interactions such as these may have arisen numerous times evolutionarily to help establish or refine patterning events in different tissues and structures. The common protostome/deuterostome ancestor must have possessed orthologs of these genes, but it is not at all clear how they deploy these bilateral molecular components of dorsal-ventral axis specification (Lowe and Wray, 1997). We are currently attempting to isolate these orthologs in both cnidarians and ctenophores to see whether bilaterian patterning genes have related roles in these diploblastic phyla.

SUMMARY

While some aspects of early development are shared in the embryos of cnidarians and ctenophores, similarities are lost quickly after the first cleavage division. Ctenophores display a stereotyped cleavage program that generates cells in distinct positions with respect to other cells within the embryo and segregates developmental potential into defined lineages. Inductive ability is also redistributed into distinct cell lineages in ctenophore embryos and it is likely that the coordinated deployment of inducing activity, resulting in the formation of "organizing centers," may be one of the fundamental inventions of metazoan developmental programs that allowed for the establishment and exploitation of bilaterally symmetrical body plans (Fig. 2). The extent to which such changes in the early cleavage program have led to the radiation of diverse metazoan phyla exhibiting bilaterally symmetrical body plans, or whether these events are related to changes in life history strategies, remains unclear. One way of understanding these changes is to learn more about the molecular basis of axis specification in the "Radiata," as virtually nothing is known about the evolution of the dorsal-ventral axis or the relationships between the oral-aboral or anterior-posterior axes in these animals. While we can speculate on these evolutionary events, the mechanistic basis for body plan evolution underlying the transition from radial to bilateral symmetry will be difficult to interpret until metazoan realaships are known.

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