

Key Transitions in Animal Evolution
Edited by Rob DeSalle and Bernd Schierwater
Science Publishers 2010
Pages 175–196
Print ISBN: 978-1-57808-695-5
eBook ISBN: 978-1-4398-5402-0
DOI: 10.1201/b10425-11

Chapter 8

Basal Metazoan Sensory Evolution

D.K. Jacobs,¹ D.A. Gold,* N. Nakanishi,* D. Yuan,* A. Camara,*
S.A. Nichols,² and V. Hartenstein³*

Introduction

Cnidaria have traditionally been viewed as the most basal animals with complex, multicellular structures dedicated to sensory perception. However, sponges also have a surprising range of the genes required for sensory and neural functions in Bilateria. We develop arguments explaining the shared aspects of developmental regulation across sense organs and between sense organs and other structures, focusing on explanations that involve divergent evolution from a common ancestral condition. In Bilateria, distinct sense-organ types share components of developmental-gene regulation. These regulators are also present in basal metazoans, suggesting evolution of multiple bilaterian organs from a smaller number of antecedent sensory structures in a metazoan ancestor. More specifically, we hypothesize that developmental genetic similarities between sense organs and appendages may reflect descent from closely associated structures, or a composite organ, in the common ancestor of Cnidaria and Bilateria, and we argue that such similarities between

*Department of Ecology and Evolutionary Biology, UCLA, 621 Young Drive South, Los Angeles CA 90095-1606.

¹Department of Molecular, Cellular and Developmental Biology, UCLA, 621 Young Drive South, Los Angeles CA 90095-1606.

²Department of Molecular and Cell Biology, 142 Life Sciences Addition, University of California, Berkeley, CA 94720.

E-mail: djacobs@ucla.edu

bilaterian sense organs and kidneys may derive from a multifunctional aggregations of choanocyte-like cells in a metazoan ancestor. We hope the speculative arguments presented here will stimulate further discussion of these and related questions.

The word “animal” implies muscle-driven motility coordinated by neural integration of sensory stimuli, which is produced in specialized multicellular sensory structures. Consequently, a number of sets of questions spring to mind when considering evolution of Metazoan sensation: Where on the tree of animal life did the first sense organs evolve? Do sense organs share a common evolutionary origin with other structures or organs? What type of sense organ evolved first and how are different classes of sense organs related to one another? Are bilaterian sense organs related to the sensory features in the more basal radiate taxa? Does the placement of Scyphozoa and Hydrozoa together in a medusozoan group support a derived condition for cnidarian sense organs? How does evidence suggesting common origin of bilaterian and cnidarian sense organs relate to the presence of bilaterian-like dorso-ventral axial organization in Cnidaria?

Not all of the preceding questions can be definitively answered at this time. However, developmental gene-expression studies, genome sequencing, and expressed-sequence-tag studies are shedding light on some of these issues. Interestingly, the initial answers to these questions are not always consistent with *a priori* expectations. For example, one might expect that evolution of genes thought to be explicitly involved in the development of sense organs would coincide with the evolution of the radiates, as Cnidaria and Ctenophora are the most basally branching lineages with specialized sense “organs”. This expectation is not met; regulatory genes involved in sense-organ development in “higher” Metazoa are present more basally in sponges, as are genes considered essential for synaptic function. Although not explicitly muscular or neural, sponges exhibit coordinated contraction as well as coordinated cessation of pumping. Thus, a view of sponges as more active is replacing an older perception that held sponges to be virtually “inanimate”.

In this work we touch on the features that distinguish sense organs, independent of classic definitions. We then consider the questions listed above in the context of the basal branches of the metazoan tree, focusing on the cnidarians and sponges. In cnidarians we address the relationship between cnidarian and bilaterian sensory structures, as well as shared aspects of sense organs and appendages. In the sponges we discuss the possible evolutionary antecedents of sense organs. Lastly we consider how different reconstructions of the metazoan tree could effect these interpretations. The speculative hypotheses presented here emphasize differential persistence and modification of an ancestral condition, rather

than invoking wholesale “cooptation” of genes, as an explanation for conflicting patterns of gene expression and morphology observed across the metazoan tree. In each instance considered, many other hypotheses could be advanced, and we encourage others to generate specific competing hypotheses.

What do Sense Organs Have in Common ?

Cells generally have an ability to assay aspects of their surroundings. However, multicellular organisms have the challenge of differential exposure of cells to external and internal environments, as well as the opportunity to have cells with specialized sensory functions. Sensory structures that form part of the epidermis are found in all animal phyla from cnidarians onward. In cnidarians and some basal bilaterian groups (e.g. acoels, platyhelminths, nemertines), sensory structures consist of “naked” sensory neurons whose dendrite is formed by a modified cilium (Chia and Koss 1979). The cell bodies of sensory neurons are often sunken beneath the level of the epidermis, or can even reside within the central nervous system. From these “naked” sensory neurons one distinguishes sensilla and sensory organs. Sensilla constitute individual sensory neurons, or small arrays of sensory neurons, which are integrated with specialized non-neuronal cells that typically function in particular sensory modalities, such as light reception, mechanoreception (auditory/inertial/touch/stretch/vibration), and chemoreception (taste/smell). Finally, sense organs are large assemblies of sensory neurons and non-neuronal cells that form macroscopic structures. Highly developed sensory organs are widespread and exist for all sensory modalities in bilaterians. In some cases, such as the compound eyes and auditory organs of arthropods, arrays of contiguous sensilla are integrated into large sensory organs. In this view “sense organs” already exist in cnidarians in the form of eyes and statocysts, despite the lack of mesoderm often invoked as a required condition for organ systems. In many instances, sensory organs and sensilla coexist with naked sensory neurons in the same animal. The sensory neurons of a sensory organ or sensillum usually bear cilia and/or microvillar structures on their apical surfaces, and these surfaces are often modified into complex membrane features (e.g. Fain 2003). Photo-reception and chemo-reception involve seven-pass transmembrane G protein-coupled receptors (GPCRs), and mechanical stimuli require membrane-bound ion channels (other sensory-cell types can detect ionic concentrations or electrical fields). Such sensory neurons then communicate by electrical potential, either through axons that are components of the sensory cells themselves (the typical invertebrate condition), or via synapses on the cell bodies to adjacent neural cells (a frequent vertebrate condition, as in the hair cells of the inner ear).

It is important to note that not all GPCRs are involved in photo- and chemo-sensory organs or “sensory” perception. Multiple independent classes of these receptors are involved in synaptic, hormonal, and developmental signaling internal to the organism (e.g. <http://www.sdbonline.org/fly/aignfam/gpcr.htm>), and the proliferation of multiple classes of GPCRs appears to be a critical distinctive feature of animals relative to other eukaryotes (<http://drnelson.utm.edu/MHEL.7TM.html>, Alvarez 2008, Römpler et al. 2008). Thus, sense organs are distinct in the particular application of GPCRs to external chemical and photoreception.

Despite these underlying similarities uniting the different sensory organs, traditional morphological comparisons have suggested that many of these structures evolved independently in multiple classes of metazoans (e.g. Salvini-Plawen and Mayr 1977). This view has been changing, largely in part to shared aspects of developmental gene expression in sense organs across the bilaterian tree, and across classes of sensory structures in a single animal. We discuss aspects of this shared genetic regulation in Bilateria; we then explore how these bilaterian-based inferences play out when compared to the limited cnidarians and sponge information. Our primary objective is to treat the range of multicellular sensory structures rather than naked sensory cells or simple sensilli.

Common Aspects of Sense-Organ Developmental Gene Regulation in Bilaterians

A suite of interactive developmental regulatory genes are highly conserved in sensory organogenesis, both between the different sensory systems, and between diverse bilaterian clades. For example, the basic helix-loop-helix gene *atonal* and its multiple vertebrate homologues are expressed in, and function in, the development of virtually all sense organs in *Drosophila* and vertebrates. *Atonal* is required for the development of the placodally derived eye, ear, and nose in vertebrates (Baker and Bronner-Fraser 2001). In *Drosophila*, *atonal* defines sense organs that consist of closely stacked sensory units, such as chordotonal organs found in stretch receptors, auditory organs, or the ommatidia of the insect compound eye (e.g. Jarman and Ahmed 1998). Initiation of development in these organs has been traced to the 3' cis region of *atonal*; only after *atonal* expression in the imaginal disks do other “master” genes, such as *eyes absent*, specify which particular sense organ will develop (Niwa et al. 2004) suggesting that multiple sensory systems evolved from a single undifferentiated, *atonal*-dependant structure, an idea that will be expanded upon later in this text.

In addition to *atonal*, a number of other genes, initially identified by the loss of eyes in *Drosophila* mutants, function in the regulatory

cascades governing the development of multiple classes of sense organ. These include *eyes absent* and *dachshund*, as well as members of the *Six* gene-family—a distinctive group of homeodomain-containing genes that includes *sine oculis* and *optix*. In addition, genes such as *Brain3* are required for specifying aspects of sensory-cell and sensory-nerve-cell differentiation in multiple classes of sense organs (auditory, olfactory and visual). Like *atonal*, these downstream regulators are conserved throughout the bilateria, and retain functions similar to *Drosophila*. For example, vertebrate placodes, the regions of ectoderm that give rise to sensory systems in the head, are defined and differentiated by members of the *Six* and *Eya* families, among other genes (Schlosser 2007). Mouse *Brain3* mutants are deaf and blind, and lack balance due to the absence of hair cells in the semicircular canals (e.g. Pan et al. 2005). Over-expression studies illuminate some of the commonality and combinatorial function of these genes. Famously, expression of the vertebrate homologue of *eyeless* (*PAX6*) successfully rescues eyes in *eyeless* mutants of *Drosophila*. However, over-expression experiments (that deliver the gene product throughout the organism) convert chordotonal organs to eyes (e.g. Halder et al. 1995). This conversion illustrates the shared developmental genetic regulation present in multiple classes of sense organ, as well as the role that Pax genes, such as *eyeless*, play in determining a subset of sense organs that includes eyes (e.g. Schlosser 2006). Thus a substantial list, including upstream regulatory genes and downstream genes with sensory-cell-type specificity, are common features of a wide range of sensory organs (Schlosser 2006) provides a summary of shared regulatory-gene control across vertebrate sensory structures).

Sharing of Developmental Regulatory Genes Across Systems

The preceding section presented a picture of the regulation of sense-organ development across divergent bilaterians. However, additional complexities intrude on this seemingly rational hierarchical organization. Developmental genes often serve multiple functions, thus hypotheses regarding common ancestry of function with distantly related organisms are not necessarily straightforward. They require attention to other lines of evidence that may suggest which facets of expression are likely to reflect shared ancestry. Many of the genes involved in the development of **sensory** organs are also involved in the development of structures that are not, or might not, typically be considered sense organs. These cases can be divided into: (1) cases with obvious functional and developmental connections to sense organs, such as nerve and muscle development, and (2) those where a developmental connection to sensory structures is less apparent, such as kidney development. Common attributes of distinctly

different organs are often dismissed as cooptation, but this is too easy; how such cooptation occurs is critical to understanding evolution. We argue that whether considered cooptive or not, overlap of gene function likely reflects aspects of shared ancestry of some components of the system, and that this common origin may be supported by examination of the basal lineages. We first touch on the “expected example” of nerve and muscle development, before considering three more challenging examples where unexpected structures share genetic overlap with sensory organs: the pituitary gland, the kidneys, and invertebrate limbs. We argue that these seemingly unrelated structures aren’t as distinct as they appear to be, and that pituitary glands, kidneys, and invertebrate limbs share attributes, and potentially ancestry, with sensory organs.

The relationship between sensory system, nervous system and muscle development

Overlap of expression of sense-organ regulatory genes with muscles and nerves is perhaps to be expected, given the functional and synaptic connections between these systems. In addition, gene duplication appears to have generated multiple players with separate functions in sensory cells, nerves and muscles. There are many examples of this overlap in groups of genes that evolved basal to the radiation of bilaterians. The Six gene classes *sine oculis* and *optix* are primarily involved in the development of sense organs in *Drosophila*, while the class *myotonix* is primarily involved in muscle development. In the NK2 homeodomain genes, *tinman* and *bagpipe* are involved in the differentiation of cardiac and smooth muscles, while *vnd* functions in the development of the medial nervous system (discussed in Jacobs et al. 1998). In Vertebrates, separate copies of Brain3 appear to have distinct functions, seemingly coincident with the division of neural and sensory cell types in the vertebrate nervous system, relative to the single neurosensory cell that performs this combined function in most invertebrate sensory neurons. The above examples of gene family function and gene duplication suggest some of the typical and more prosaic ways in which genes involved in sense-organ developmental regulation appear to “coopt” new functions in their evolutionary history. However, this cooptation does not preclude the possibility that these sensory, neural, and muscular controls are related by a common ancestral cell-type. As mentioned above, invertebrate sensory cells also have neuronal processes, while vertebrates sensory cells and neurons are distinct. This idea will gain further support when we discuss more basally branching taxa, such as the cnidarians and sponges.

The relationship between sensory system and pituitary development

A number of sense-organ-specific genes such as the Six genes, as well as *eyes absent*, and *dachshund* homologues (e.g. Schlosser 2006) are expressed in the pituitary as well as in sensory structures, as is the POU gene PIT1, the most closely related POU gene to Brain3. This developmental-genetic overlap between sensory systems and the pituitary gland is surprising on its face, but proves consistent with the evolution of the adenohypophyseal component of the pituitary, from an external chemosensory to an internal endocrine organ in chordate lineage (e.g. Gorbman 1995, Jacobs and Gates 2003). Thus, the presence of the gene Pit1 in more basal taxa, including cnidarians and sponges (Jacobs and Gates 2003), is consistent with an evolutionarily antecedent to the vertebrate pituitary, perhaps involved in external reproductive communication. And like vertebrate sensory organs, the pituitary is placoidally derived. Other structures derived from cephalic placodes in vertebrates share aspects of regulation with formal sense organs (Schlosser 2006) and also likely have a common evolutionary origin with sensory structures.

The relationship between sensory system and kidney development

Both sense organs and kidneys express the same suite of regulators in development, and there are a number of diseases that effect the ear and kidney in particular leading to the biomedical term otic-renal complex (see Izzedine et al. 2004 for review). In this unexpected case—the commonality of kidneys and sense organs—we argue below that this could reflect cellular organization in sponges, in which groupings of choanocytes may serve multiple functions and subsequently evolved into the *sense organs and kidneys* in bilaterians. We advance this particular argument based on the initially surprising commonality of sensory regulation and disease in distinctly different organs. However, this does not limit the possibility that many other systems in higher Metazoa may also have common origins; given the small set of differentiated cell and tissue types found in sponges, this may be necessarily the case. For an additional example, the expression of *atonal* homologues associated with the neuroendocrine cells of the gut (e.g. Yang et al. 2001, Bjerknes and Cheng 2006) also suggests to us that they could logically be derivative from the choanocyte cell component.

The relationship between sensory system and limb development

Vertebrate limbs are novel derived feature of gnathostome vertebrates; consequently, the pharyngeal arches are the vertebrate structure most directly related to invertebrate appendages (e.g. Shubin et al. 1997). So in an evolutionary context, the inner ear, derived from the pharyngeal

arches, is an appendage-derived sensory structure. Moreover, common developmental gene expression and motor proteins, such as prestin and myosin VIIa, function in both vertebrate “ears” and the hearing organs found in the joints of *Drosophila* appendages (e.g. the Johnston’s organ; Todi et al. 2004, Kamakouchi et al. 2009) arguing for evolutionary continuity through a shared ancestral auditory/inertial or comparable mechano-sensory structure (Boekhoff-Falk 2005, Fritsch et al. 2006) borne in this “appendage” context.

Besides the appendage joint/hearing organ association found in *Drosophila*, many other examples of sensory-appendages exist in the fly. For example, fringe and associated regulators function along the equator (akin to a dorso-ventral compartment boundary) of the *Drosophila* eye, as well as in the evolutionarily secondary *Drosophila* wing, where they are responsible for defining the wing margin, which itself bears a row of sensory bristles. The eye imaginal disk in *Drosophila* is a positional equivalent serial homologue of the walking appendages. There is a well-documented relationship between eye, antennae, and appendage formation in *Drosophila*, and ectopic expression of *Antennapedia* can convert *Drosophila* antennae into second thoracic legs (Schneuwly et al. 1987), as well as stop eye development through mutual inhibition with *eyeless* (Plaza, 2001). The fly antenna, an “olfactory appendage” with multiple odorant receptors (Vosshall et al. 1999, Laissue et al. 2008) as well as an auditory and gravity measuring structure (Todi et al. 2004, Kamakouchi et al. 2009), shares the same imaginal disk with the compound eye. Misexpression of one gene, *Dip3*, is sufficient to convert eyes into antennae (Duong et al. 2008). More generally, homology of anterior sensory structures with more posterior appendages in the segmental series are standard inferences across the arthropods, and can be further supported by the presence of chemosensory (Zacharuk 1980) and mechanosensory (McIver 1985, Keil 1997) sensilla on the posterior appendages.

Finally, this sensory-appendage overlap is not unique to the arthropods. The presence of eyes on the parapodia in some species of polychaete (e.g. Verger-Bocquet 1981, Purshce 2005) documents evolutionary conversion of limbs to sense-organ-bearing structures. They are evolutionary “phenocopies”, producing phenotypes comparable to those engendered by *eyeless* over-expression that convert limb-borne chordotonal organs to eyes, as was discussed above. The presence of eyes on the terminal tube feet (appendages) near the ends of the “arms” (axial structures) of sea stars (e.g. Mooi et al. 2005, Jacobs et al. 2005) provides an instance in yet another bilaterian phylum where sense organs and are associated with “appendages”.

Cnidaria: Homology of Medusan Sensory Structures with the Bilateria

Having considered these common aspects of bilaterians development, we now compare this information to the cnidarian condition. The outgroup status of Cnidaria should help polarize the evolutionary changes in Bilateria, testing whether the relationships discussed above are in fact ancestral or derived. Sense organs of the cnidarian medusa are highly developed and distributed across scyphozoan, hydrozoan and cubozoan lineages. The rhopalium, the sense organ bearing structure of Scyphozoa and Cubozoa (a modified group within the scyphozoans), is borne on the margin of the bell in the medusa, and contains the statocyst and eyes. The rhopalia of cubozoan medusae contain eyes with lenses, the most dramatic of cnidarian sense organs. These eyes presumably facilitate swimming in these very active medusae with extremely toxic nematocysts. Other cnidarian eyes are simpler. These eyes tend to be simple eyespots or pinhole camera eyes that lack true lenses (see Martin 2002, Piatagorsky and Kozmik 2004 for review). In the scyphozoan *Aurelia*, the statocyst is effectively a “rock on a stalk”, with a dense array of mechanosensory cells that serve as a “touch plate” at the base of the stalk where it can contact the overlying epithelium of the rhopalium (e.g. Spangenberg, et al. 1996, Arai 1997).

Several studies document expression of regulatory genes in Cnidaria that typically function in the development of bilaterian sense organs. These studies document a common aspect of gene expression, albeit with significant variation. In the scyphozoan *Aurelia* a homologue of *sine oculis* is expressed in the rhopalia (Bebeneck et al. 2004), as is the case for Brain3 (Jacobs and Gates 2001) and *eyes absent* (Nakanishi et al. in prep). Six-class genes are also expressed in the development of the eyes in the hydrozoan *Cladonima* (Stierwald et al. 2004). These sorts of data, taken together, provide a substantial argument for a shared ancestry between bilaterian and Cnidarian sense organs generally. Shared ancestry of specialized classes of sensory organs, such as eyes, also appears likely. The evolution of the light-sensitive GPCR opsins is complex, as there are many functions and families of the related GPCR receptors. However, recent analyses support a sister taxon relationship between the ciliary opsins of Cnidaria and those of bilaterians (e.g. Suga et al. 2008) strongly suggesting a shared ancestry of this major mode of photo-sensation.

In Cubozoa a paired-class gene has been identified that is expressed in sense-organ development (Kosmik et al. 2003). Interestingly, this PaxB gene does not appear to be a simple homologue of *eyeless/Pax6*, as it contains an *eyeless/Pax6* type homeodomain combined with a paired domain typical of PAX 2/5/8—a regulatory gene more closely associated with ear development that is also expressed in statocysts in mollusks (O'Brien

and Degnan 2004). Statocysts are ear-like in their inertial function and are localized with the eye in the cnidarian rhopalium. Given that cubozoan statocyst expresses PAXB along with the eye, a PaxB-type gene appears to have undergone duplication and modification in the evolution of the bilaterian condition such that eyes and ears are differentially regulated by separate PAX6 and PAX 2/5/8 genes. This evolution in the ancestry of *eyeless/Pax6* contrasts with a number of other sense-organ regulatory genes such as *sine oculis* (Bebeneck et al. 2004), Brain3 (Jacobs and Gates 2001) and *eyes absent* (Nakanishi et al. *in prep*), all of which appear to be extremely similar in their functional domains to specific bilaterian homologues. Thus, *eyeless/PAX6* may have evolved more recently into its role in the eye development than other regulatory genes that also function in other sense organs.

The Issue of Exclusivity of Sensory Structures to the Medusa Stage

In opposition to the above arguments for a shared ancestry of bilaterian-cnidarian sensory systems is the perception that cnidarian sense organs are exclusive to the medusa, and that the medusan phase is derived given the basal placement of the Anthozoa, which lack such a stage in their life cycle (e.g. Bridge et al. 1992, Collins et al. 2006). However, a variety of arguments limit the strength of support for completely *de novo* evolution of cnidarian sense organs. Neither the polyp nor the sense-organ containing medusa are present in outgroups, consequently the power of tree reconstruction to resolve the presence or absence of medusa or polyp is minimal (Jacobs and Gates 2003). This, combined with the frequency of loss of the medusa phase in hydrozoan lineages, limits confidence in the inferred absence of a medusa-like form in the common ancestor. In addition, features that may merit consideration as sense organs are present in planula and polyps. In particular, statocysts are found in some unusual hydrozoan polyps (Campbell 1972) and ocelli associate with the tentacle bases in some stauromedusan (Scyphozoa) polyps (Blumer 1995). Thus, the emphasis on the medusan phase of the life history may be unwarranted.

Numerous opsins have been discovered in the anthozoan *Nematostella*, and from the hydrozoan *Hydra*, neither of which has “eyes” in the traditional sense (Suga et al. 2008). Suga et al. (2008) have shown the expression of comparable ciliary opsins in the eyes of the hydrozoan *Cladonema* as well as in other potentially sensory structures such as tentacles and the manubrium (oral structure), a point developed further below.

Additional Cnidarian Sensory Systems

The cnidocytes of Cnidaria are innervated (e.g. Anderson et al. 2004) and have triggers that respond to sensory stimuli. In some instances

they synaptically connect with adjacent sensory cells (Westfall 2004). Thus, cnidocytes are, at once, a potential source of sensory stimulation and, presumably, modulate their firing in response to neuronal stimuli (e.g. Anderson et al. 2004). Having acknowledged this complexity, we set it aside and limit the discussion to the integration of more traditional sensory cells into what may be considered sense organs.

In the planula larvae of Cnidaria, FMRF-positive sensory cells are found in a belt running around the locomotory “forward” end (aboral after polyp formation) of the planula ectoderm (e.g. Martin 1992, 2002). The axons of these cells extend “forward” along the basement membrane of the ectoderm and are ramified, forming what appears to be a small neuropile at the aboral pole of the planula. This feature varies among taxa; in hydrozoans such as *Hydractinia*, the array of sensory cells appears closer to the aboral end of the elongate planula. There is also ontogenetic variation in which the sensory cells move closer to the aboral end prior to settlement (Nakanishi et al. 2008). Strictly speaking, the sensory neurons of the cnidarian planula correspond to the “naked” sensory neurons discussed previously; however, one might consider dense arrays of such chemoreceptive and/or mechanoreceptive neurons as “precursors” of sense organs. Expression data for *atonal* in hydrozoan planulae (Seipel et al. 2004) also suggest that this integrated array of sensory cells could merit “sense organ” status.

The hypostome and manubrium, oral structures of the polyp and medusa respectively, may also rise to the status of sense organs. In *Aurelia* ephyrae (early medusa), sensory cells are present in rows on the edges of both the ectoderm and endoderm of the manubrium. POU genes such as Brain3 (unpublished) are expressed in the manubrium of *Aurelia*, as is a homologue of *sine oculis* (Bebenek et al. 2004). Similar *sine oculis* expression in the manubrium is evident in the hydrozoan *Podocoryne*, but this may not be the case in *Cladonema* where a related Six gene *myotonix/Six4,5* is expressed in the manubrium (Steirwald 2004). *Cladonema* does, however, exhibit manubrium-specific opsins that are distinct from those found in the eyes, gonads, or ubiquitously across the body, suggesting that the manubrium has a distinct photosensory role (Suga et al. 2008). In *Podocoryne*, limited expression of *atonal* is evident in the manubrium (Seipel et al. 2004), and PaxB is expressed in the manubrium and hypostome (Groger et al. 2000).

Tentacles as Appendages and Sense Organs

The shared developmental aspects between sense organs and appendages discussed in the bilaterians above, is also found in the Cnidaria. Cnidarian

tentacles are variable; ectoderm and endoderm layers and a central lumen connected to the gastrovascular cavity are typical of anthozoan tentacles. In contrast, polyp tentacles of scyphozoans and some hydrozoans lack a lumen; these tentacles have a single row of large vacuolated endodermal cells as the core of a slender tentacle. A variety of tentacle morphologies are also present in medusae. We discuss whether tentacles are (1) sense organs, (2) sense organ bearing structures, and (3) whether tentacles and rhopalia (that bear sense organs in scyphozoans) are alternative developmental outcomes of an initially common developmental field or program. Ultrastructural studies as well as markers such as FMRF that typically recognize sensory cells and neurons document arrays of sensory cells in tentacles that are substantially denser than those found in the body wall of the polyp or in the medusan bell. *Optix* homologues are also expressed in certain presumed sensory neurons or cnidocytes in tentacles of *Podocoryne* (Stierwald 2004). Sensory cells form concentrations at the base of the tentacle or, in some instances, at the tips of the tentacles (e.g. Holtman and Thurm 2001); these concentrations merit consideration as sense “organs”.

Sense-organ-related genes are preferentially expressed near the bases of hydrozoan tentacles; *sine oculis* and PAXB are expressed here in *Podocoryne*, a hydrozoan medusa that lacks eyes (Steirwald et al. 2004, Groger et al. 2000). Sensory gene expression associated with tentacle bases is not exclusive to medusae. In the anemone *Nematostella*, PaxB homologues are expressed adjacent to the tentacles (Matus et al. 2007). In addition, the base of the tentacle is the locus of ocelli in some unusual polyps as discussed above (Blumer 1995). Thus, a developmental field specialized for the formation of sensory organs appears to be associated with the bases of cnidarian tentacles, but concentrations of sensory cells at the end of the tentacle also occur, as is the case in the polyp tentacles of the hydrozoan *Coryne* (e.g. Holtmann and Thurm 2001).

In *Hydra* an *aristaless* homologue is expressed at the base of tentacles (Smith et al. 2000), comparable to the proximal component of expression seen in arthropod limbs (Campbell et al. 1993). TGF beta expression always precedes tentacle formation in tentacle induction experiments (Reinhardt et al. 2004) and continues to be expressed at the tentacle base. Both *decapentplegic* and *aristaless* are involved in the localization and outgrowth of the appendages in flies (e.g. Campbell et al. 1993, Crickmore and Mann 2007). Thus there are also common aspects of bilaterian appendage and cnidarian tentacle development.

As noted above, in typical Scyphozoa, rhopalia alternate with tentacles in a comparable bell-margin position; in Hydrozoa, sense organs associate with the tentacle bases. Overall, there is support for a common appendage/sense-organ field in Cnidaria comparable to that evident in

Bilateria as discussed above. In those hydrozoans with a medusa stage, many have eyes associated with the tentacle base. The relative position of the eye and tentacle appears to be evolutionarily plastic; the necto-benthic *Polyorchis penicillatus* feeds on the bottom and its eyes are on the oral side, presumably aiding in prey identification on the bottom, whereas the nektonic *P. montereyensis* (e.g. Gladfelter 1972) has eyes on the aboral side of the tentacle, presumably aiding in identification of prey in the water column. Nevertheless, the hydrozoan eye appears to be closely associated with the base of the tentacle. In Scyphozoa there are typically eight rhopalia that alternate with eight tentacles around the bell margin. Cubozoa have four rhopalia that similarly alternate with tentacles. Although, there are exceptions to this alternating tentacle/rhopalia pattern (e.g. Russell 1970) they appear to be derived. Thus appendages in the form of tentacles and the sense organ bearing rhopalia occupy a similar position/field that appears to assume alternative fates in development. This is consistent with the arguments relating appendages and sense organs in Bilateria developed above, and relates to our discussion of tentacles considered as appendages as well as sense organs in cnidarians.

Sensory Attributes of Sponges

Sponges are thought to constitute the most basal branch, or branches, of the animal tree, and a progressivist view of evolution has long treated them as primitively simple (Jacobs and Gates 2003). Yet, there is increasing evidence that sponges are not as simple as often anticipated: (1) some sponge lineages exhibit coordinated motor response to sensory stimuli and others possess an electrical-conduction mechanism; (2) sponges have genes encoding proteins that function in a range of bilaterian developmental processes; and (3) sponges have many of the genes employed in the development of sense organs. The presence of genes known to function in eumetazoan sense-organ development in a group lacking formal sense organs presents interpretive challenges. Certain sets of larval cells or the grouping of choanocytes into functional arrays represent possible sponge structures potentially related to eumetazoan sense organs. We discuss these briefly and explore the possibility that multiple organs, including kidneys and sense organs, may share ancestry with ensembles of choanocytes.

Motor Coordination of Sponges

Sponges exhibit contractile behaviors (reviewed by Leys and Meech 2006, Elliot and Leys 2003). In the small, freshwater sponge *Ephydatia*, an inhalant expansion phase precedes a coordinated contraction that forces water out of the osculum. This contractile activity generates high-velocity flow in the finer channel systems that then propagate toward the osculum.

Effectively, this seems to be a “coughing” mechanism that eliminates unwanted material, chemicals or organisms from the vasculature. Sponges are known to have specialized contractile cells, termed myocytes, which have been compared to smooth-muscle cells; however, other epithelial cell types (pinacocytes, actinocytes) contribute to contractile behavior (reviewed by Leys and Meech 2006).

Given that sponges lack formal synapses it is worth noting that non-synaptic communication between cells via calcium waves can occur through a variety of mechanisms. One such class of mechanism involves gap junctions or gap junction components, but these have yet to be documented in sponges and are presumed absent. Others involve the vesicular release of molecules such as ATP, which can operate through receptors associated with calcium channels or through specific classes of GPCRs (see North and Verkohtsky 2006 for review of purinergic communication). Such receptors are known to permit non-synaptic intercellular communications in nerves and non-neuron components such as between glial cells. In hexactinellids “action potentials” that appear to involve calcium propagate along the continuous membranes of the syncytium that constitutes the inner and outer surface of these sponges (Leys and Mackie 1997). This propagation of signals along the syncytium permits rapid coordinated choanocyte response to environmental stimuli in hexactinellids. In other classes of sponges, propagation of information appears to involve calcium dependent cell/cell communication (Leys and Meech 2006). Mechanisms of this sort, involving non-synaptic vesicular release of signaling molecules and a “calcium wave” propagation, seem broadly consistent with available information communication in cellular sponges reviewed in detail by Leys and Meech (2006).

Sensory Systems in Sponges

The ring-cells around the posterior pole (relative to direction of motion) of the parenchyma larva of the demosponge *Amphimedon* has been shown to be photosensitive and to respond to blue light (Leys et al. 2002, see Maldonado et al. 2003 for observations on other demosponge larvae).

These cells effectively steer the sponge, using long cilia providing for a phototactic response. Sakarya et al. (2007) document that flask cells of larval sponges express proteins involved in postsynaptic organization in Bilateria, and speculate that these cells are sensory. These larval sensory attributes are of interest as larvae provide a likely evolutionary link with the radiate and bilaterian groups (e.g. Maldonado 2004).

Groups of choanocyte cells in adult sponges also bear some similarity to eumetazoan sensory structures as: (1) choanocytes are crudely similar in morphology to sensory cells, particularly mechanosensory cells; (2) the

deployment of sponge choanocytes in chambers is similar to the array of sensory cells in sense organs; and (3) choanocytes are a likely source of stimuli that produce the contractions and electrical communications as noted above. Choanocytes of sponges and choanoflagellates present a cilium/flagellum surrounded by a microvillar ring on the apex of the cell, which bears at least superficial similarity to the typical organization of many sensory cells, such as those of the ear (e.g. Fritsch et al. 2006, Fain 2003). Clearly chemical signals in the water can induce contractile responses in demosponges (e.g. Ellwanger et al. 2007, Leys and Meech 2006). In addition it appears likely that mechano and chemosensory responses to particles would be necessary for the feeding function of the choanocyte and that communication between adjacent choanocytes in the choanosome structure would also be essential to feeding. Feeding behavior appears coordinated across sponges rather than just within choanosomes as different types of particles are preferred under different circumstance (e.g. Yahel et al. 2006, 2007).

Genetic Control of Sponge Neural Development

The molecular complexity of sponges exceeds that expected based on their presumed “primitive” nature. Nichols et al. (2006) reported a range of extracellular matrix proteins as well as components of the major intercellular signaling pathways operative in metazoan development from their EST study of the demosponge *Oscarella*. Larroux et al. (2006, 2008) reported a diverse array of homeodomains and other DNA-binding regulatory genes from the demosponge *Amphimedon queenslandica* (formerly *Reneira*). Thus, sponges possess a significant subset of the equipment used to differentiate cells and tissues in Bilateria and Cnidaria (see Ryan et al. 2006 for a recent survey of cnidarian homeodomains from the *Nematostella* genome and Simionato et al. [2007] for survey of bHLH regulators across Metazoa, including cnidarians and demosponge genomic data).

Recent work by Sakarya et al. (2007) documents the presence of “post-synaptic” proteins and argues that these proteins are organized into a post-synaptic density comparable to that found in eumetazoan synapses. This suggests surprising functionality given the absence of formal synapses in sponges. An EST study of the demosponge *Oscarella* provides additional support for the presence of molecular components that are required for vesicle related signaling function (Jacobs et al. 2007). These recent observations in sponges suggest a high activity of equipment involved for vesicle transport, and the presence of some synaptic and developmental signaling components typically associated with bilaterian neural systems.

Turning to sense-organ-associated regulators, *sine oculis* homologues are present in all classes of sponges (Bebeneck et al. 2004), as are homologues of Brain3 (Jacobs and Gates 2001, 2003 & unpublished). Similarly, relatives of *atonal* are present in demosponges (Simionato et al. 2007). Richards et al. (2008) demonstrated expression of Notch-Delta signaling and atonal-like basic helix loop helix neurogenic genes in the Demnosponge *A. queenslandica*. NK2 genes play important roles in bilaterian mesoderm and neural differentiation (Jacobs et al. 1998), and it has recently been argued that the presence of NK2 gene expression in Homoscleromorph choanocytes is consistent with an ancestral neural/sensory function of this cell type (Gazave et al. 2008). Thus, sponges, and associations of choanocytes in particular, appear to have many components of the regulatory gene cascades associated with sense-organ development in Eumetazoa.

Choanocytes as the Ancestral Sensory Structure

As noted above, vertebrate sensory organs have a surprising amount in common with the kidney; both, for example, express Pax6, *eyes absent* and *sine oculis* in development, and numerous genetic defects affect both structures (e.g. Izzedine et al. 2004). Consideration of sense organs, and organs that eliminate nitrogenous waste, both as evolutionary derivatives or relatives of a choanocyte chambers, may help explain these commonalities. The fluid motion engendered by choanocyte chambers renders these structures the central agency in nitrogenous waste excretion, in addition to their other functions (e.g. Laugenbruch and Weissenfels 1987); vacuoles involved in the excretion of solids following phagocytic feeding presumably represent a separate aspect of waste disposal (e.g. Willenz and Van De Vwer 1986). In a number of bilaterian invertebrates, nitrogen-excreting protonephridia consist of specialized ciliated flame cells that generate the flow and pressure differential critical for initial filtration, much as sponge choanocytes generate flow in feeding. These systems appear intermediate between choanocytes and metanephridia that rely on blood pressure for filtration (e.g. Bartolomaeus and Quast 2005). Thus we draw attention to the potential evolutionary continuity of function and structure between associations of choanocytes and protonephridia, and ultimately metanephridia. These are of interest in the context of the potential for explaining the common features of sense organs and kidneys (e.g. Izzedine et al. 2004). Such explanations are necessarily speculative, but will soon be subject to more detailed test with an increasing knowledge of gene expression and function in sponges. It should also be noted that this argument does not negate the possibility that a number of other structures such as the neurendocrine structure of the gut epithelium, as mentioned above, might also derive from or share ancestry with the choanosome.

Tree Topology

Tree topology is critical to evolutionary interpretation of the events surrounding the evolution of sensory systems in the basal Metazoa. Most continue to treat sponges as basal in the Metazoa (Srivastava et al. 2008, Ruiz-Trillo et al. 2008). Other works (Borchiellini et al. 2001, Medina et al. 2001, Sperling et al. 2007) suggest that Eumetazoa derive from a paraphyletic sponge group. These analyses tend to place the Eumatazoa as sister to the calcareous sponges. Sponge paraphyly implies that the ancestral eumetazoan was sponge-like, with choanocytes and other broadly distributed attributes of sponges, lending credence to arguments that choanosome development may have contributed to the evolution of sensory structures as argued above (Sperling et al. 2007). Additionally, unique demnospunge derived steranes constitute the earliest evidence of animals in the rock record, potentially supporting earlier evolution of sponges relative to other animal groups (Love et al. 2009). The placement of Cnidaria as sister to the Bilateria has also received recent support in other studies (e.g. Halanych 2004, Baguñā et al. 2008), as well as the relationships between the classes of cnidaria as discussed above. However, one recent analysis placed Ctenophores basal on the animal tree (Dunn et al. 2008), while others have suggested that Placozoans are basal in a clade composed of Placozoa, Cnidaria, Ctenophora and the sponges, which itself is sister to the Bilateria (Schierwater et al. 2009, Signorovitch et al. 2007, Blackstone 2009). The enigmatic Placozoa are certainly of interest, as they may provide information on the nature of the stem of the metazoan tree and potentially permitting interpretation of Vendian (late Precambrian) fossils (e.g. Conway-Morris 2003). The large size of the placozoan mitochondrial genome is comparable to those found in protista, suggesting that Placozoa may be the most basal branch of the Metazoa. Conversely, Ruiz-Trillo et al. (2008) placed the Placozoans as sister to the bilaterians. Ribosomal genes place Placozoa in a variety of basal positions (e.g. Borchiellini et al. 2001, Halanych 2004), but are largely consistent with the basal placement and/or paraphyly of sponges discussed above. There is evidence for PAX-like genes in the presumptively basal Placozoa (Hadrys et al. 2005), as well as basic helix–loop–helix family genes, POU-homeobox genes, and most of the processes necessary for neural formation and conduction (Schierwater et al. 2008). This is broadly consistent with the evolution of many major classes of metazoan regulatory proteins in the stem lineage, prior to the radiation of modern metazoan phyla (Derelle et al. 2007 provides a recent analysis of homeobox gene families in this context).

Whether sponges, placozoans, or ctenophores are the most basally branching members of the animal tree has limited effect on the arguments

presented in this paper, as the available evidence is pointing to a basal animal node that is complexly endowed with the regulatory apparatus that is known to function in bilateria sense organ development.

Summary

We have argued that many aspects of sense organ evolution preceded the evolution of formal organs in the triploblastic Bilateria. Clearly Cnidaria have well-developed neural and sensory features, some of which may merit treatment as “organs”. However even sponges appear to have precursory elements of sensory organization. In addition, sense-organs share attributes with endocrine structures, appendages and kidneys. We argue that these similarities are a product of derivation from common ancestral structures. In a more general sense, as one compares structures in divergent ancient lineages such as the basal lineages of the Metazoa, we feel that similarities that are the product of shared ancestry are likely to be manifest in surprising and subtle ways. Thus, neither inferences of similarity as indicative of strict homology nor dismissal of similarity as products of convergence or cooption should meet with facile acceptance.

Acknowledgements

We thank Sally Leys for discussions, Chris Winchell and anonymous reviewers for their helpful critique, and NASA Astrobiology Institute for support.

References

- Anderson, P.A.V. and L.F. Thompson, and C.G. Money Penny. 2004. Evidence for a common pattern of peptidergic innervation of cnidocytes. *Biol. Bull.* 207: 141–146.
- Alvarez, C. 2008. On the origins of arrestin and rhodopsin. *BMC Evol. Biol.* 8: 222.
- Arai, M.N. 1997. *A Functional Biology of Scyphozoa*. Chapman and Hall, London and New York.
- Baguná, J. and P. Martínez, J. Paps, and M. Riutort. 2008. Back in time: a new systematic proposal for the Bilateria. *Phil. Trans. R. Soc. B* 363: 1481–1491.
- Baker, C.V. and M. Bronner-Fraser. 2001. Vertebrate cranial placodes I. Embryonic induction. *Dev. Biol.* 232: 1–61.
- Bartolomaeus, T. and B. Quast. 2005. Structure and development of nephridia in Annelida and related taxa. *Hydrobiologia* 535: 139–165.
- Bebenek, I.G. and R.D. Gates, J. Morris, V. Hartenstein, and D.K. Jacobs. 2004. *Sine oculis* in basal Metazoa. *Dev. Genes Evol.* 214: 342–351.
- Bjerknes, M. and H. Cheng. 2006. Neurogenin 3 and the enteroendocrine cell lineage small intestinal epithelium. *Devel. Biol.* 300: 722–735.
- Blackstone, N.W. 2009. A New Look at Some Old Animals. *PLoS Biol* 7(1) e1000007.
- Blumer, M.J.F. and L.V. Salvini-Plawen, R. Kikinger, and T. Buchinger. 1995. Ocelli in a Cnidaria polyp: the ultrastructure of the pigment spots in *Stylocoronella riedli* (Scyphozoa, Stauromedusae). *Zoomorphology* 115: 221–227.

- Boekhoff-Falk, G. 2005. Hearing in *Drosophila*: Development of Johnston's organ and emerging parallels to vertebrates ear development. *Dev. Dynam.* 232: 550–558.
- Borchiellini, C. and M. Manuel, E. Alivon, N. Boury-Esnault, J. Vacelet, and Y. Le Parco. 2001. Sponge paraphyly and the origin of Metazoa. *J. Evol. Biol.* 14: 171–179.
- Bridge, D. and C.W. Cunningham, B. Schierwater, R. DeSalle, and L.W. Buss. 1992. Class-level relationships in the phylum Cnidaria: evidence from mitochondrial gene structure. *Proc. Natl. Acad. Sci. USA* 89: 8750–8753.
- Campbell, G. and T. Weaver, and A. Tomlinson. 1993. Axis specification in the developing *Drosophila* appendage: the role of wingless, decapentalegic, and the homeobox gene *aristaless*. *Cell.* 74: 1113–1123.
- Chia, F.S. and R. Koss. 1979. Fine structural studies of the nervous system and the apical organ in the planula larva of the sea anemone *Anthopleura elegantissima*. *J. Morphol.* 160: 275–297.
- Collins, A.G. and P. Schuchert, A.C. Marques, T. Jankowski, M. Medina, and B. Schierwater. 2006. Medusozoan phylogeny and character evolution clarified by new large and small subunit rDNA data and an assessment of the utility of phylogenetic mixture models. *Syst. Biol.* 55: 97–115.
- Conway-Morris, S. 2003. The Cambrian “explosion” of metazoans and molecular biology: would Darwin be satisfied? *Int. J. Dev. Biol.* 47: 505–515.
- Crickmore, M.A. and R.S. Mann. 2007. Hox control of morphogen mobility and organ development through regulation of glypican expression. *Development* 134: 327–334.
- Derelle, R. and P.L. Herve' Le Guyader, and M. Manuel. 2007. Homeodomain proteins belong to the ancestral molecular toolkit of Eukaryotes. *Evol. Dev.* 9: 212–219.
- Dunn, C.W. et al. 2008. Broad phylogenomic sampling improves resolution of the animal tree of life. *Nature* 452: 745–749.
- Duong, H.A. et al. 2008. Transformation of eye to antenna by misexpression of a single gene. *Mech. of Develop.* 125: 130–141.
- Ellwanger, K. and A. Eich, and M. Nickel. 2007. GABA and glutamate specifically induce contractions in the sponge *Tethya wilhelma*. *J. Comp. Physiol. A* 193: 1–11.
- Fain, G.L. 2003. *Sensory Transduction*. 288pp. Sinauer Associates, Inc, Sunderland, MA.
- Fritsch, B. and S. Pauley, and K.W. Beisel. 2006. Cells, molecules and morphogenesis: the making of the vertebrate ear. *Brain Res.* 1091: 151–171.
- Gladfelter, W.B. 1972. Structure and function of the locomotory system of *Polyorchis montereyensis* (Cnidaria, Hydrozoa). *Helgoland Mar. Res.* 23: 38–79.
- Gorbman, A. 1995. Olfactory origins and evolution of the brain-pituitary endocrine system: facts and speculation. *Gen. Comp. Endocrinol.* 97: 171–178
- Groger, H. and P. Callaerts, W.J. Gehring, and V. Schmid. 2000. Characterization and expression analysis of an ancestor-type Pax gene in the hydrozoan jellyfish *Podocoryne carnea*. *Mech. Develop.* 94: 157–169.
- Hadrys, T. and R. DeSalle, S. Sagasser, N. Fischer, and B. Schierwater. 2005 The Trichoplax PaxB gene: A putative proto-PaxA/B/C gene predating the origin of nerve and sensory cells. *Mol. Biol. Evol.* 22: 1569–1578.
- Halanych, K.M. 2004 The new view of animal phylogeny. *Annu. Rev. Ecol. Syst.* 35: 229–256.
- Halder, G. and P. Callaerts, and W.J. Gehring. 1995. Induction of ectopic eyes by targeted expression of the *eyeless* gene in *Drosophila*. *Science* 267: 1788–1792.
- Holtman, M. and U. Thurm. 2001. Variations of concentric hair cells in a cnidarian sensory epithelium. *J. Comp. Neurol.* 432: 550–563.
- Izzedine, H. and F. Tankere, V. Launay-Vacher, and G. Deray. 2004. Ear and kidney syndromes: Molecular versus clinical approach. *Kidney Int.* 65: 369–385.
- Jacobs, D.K. and S.E. Lee, M.N. Dawson, J.L. Staton and K.A. Raskoff. The history of development through the evolution of molecules: Gene trees, hearts, eyes, and dorsoventral inversion, pp. 323–357. *In*: R. DeSalle and B. Schierwater. [eds.] 1998. *Molecular Approaches to Ecology and Evolution*. Birkhauser, Basel.

- Jacobs, D.K. and R.D. Gates. 2001. Evolution of POU/homeodomains in basal Metazoa: Implications of the evolution of sensory systems and the pituitary. *Dev. Biol.* 235: 241.
- Jacobs, D.K. and R.D. Gates. 2001. Is reproductive signaling antecedent to metazoan sensory and neural organization? *Am. Zool.* 41: 1482–1482.
- Jacobs, D.K. and R.D. Gates. 2003. Developmental genes and the reconstruction of metazoan evolution—implications of evolutionary loss, limits on inference of ancestry and type 2 errors. *Integr. Comp. Biol.* 43: 11–18.
- Jacobs, D.K. and N.C. Hughes, S.T. Fitz-Gibbon, and C.J. Winchell. 2005. Terminal addition, the Cambrian radiation and the Phanerozoic evolution of bilaterian form. *Evol. Dev.* 7: 498–514.
- Jacobs, D.K. et al. 2007. Evolution of sensory structures in basal metazoa. *Integr. Comp. Biol.* 47: 712–723.
- Jarman, A.P. and I. Ahmed. 1998. The specificity of proneural genes in determining *Drosophila* sense organ identity. *Mech. Dev.* 76: 117–125.
- Kamikouchi, A. and H.K. Inagaki, T. Effertz, O. Hendrich, A. Fiala, M.C. Göpfert, and K. Ito. 2009. The neural basis of *Drosophila* gravity-sensing and hearing. *Nature* 458: 165–169.
- Keil, T.A. 1997. Functional morphology of insect mechanoreceptors. *Microsc. Res. Tech.*, 39(6): 506–531.
- Kozmik, Z. and M. Daube, E. Frei, B. Norman, L. Kos, L.J. Dishaw, M. Noll, and J. Piatigorsky. 2003. Role of Pax genes in eye evolution: a cnidarian PaxB gene uniting Pax2 and Pax6 functions. *Dev. Cell* 5: 773–785.
- Laissue, P.P. et al. 2008. The olfactory sensory map in *Drosophila*. *Adv. Ex. Med. Biol.* 628: 102.
- Langenbruch, P.F. and N. Weissenfels. 1987. Canal systems and choanocyte chambers in freshwater sponges (Porifera, Spongillidae). *Zoomorphology* 107: 11–16.
- Larroux, C. and B. Fahey, D. Liubicich, V.F. Hinman, M. Gauthier, M. Gongora, K. Green, G. Wörheide, S.P. Leys, and B.M. Degnan. 2006. Developmental expression of transcription factor genes in a demosponge: insights into the origin of metazoan multicellularity. *Evol. Develop.* 8: 150–173.
- Larroux, C. and G.N. Luke, P. Koopman, D.S. Rokhsar, S.M. Shimeld, and B.M. Degnan et al. 2008. Genesis and expansion of metazoan transcription factor gene classes. *Mol. Biol. Evol.* 25: 980–996.
- Leys, S.P. and G.O. Mackie. 1997. Electrical recording from a glass sponge. *Nature* 387: 29–30.
- Leys, S.P. and T.W. Cronin, B.M. Degnan, and J.N. Marshall. 2002. Spectral sensitivity in a sponge larva. *J. Comp. Physiol. A* 188: 199–202.
- Leys, S.P. and R.W. Meech. 2006. Physiology of coordination in sponges. *Can. J. Zool.* 84: 288–306.
- Love, G.D. et al. 2009. Fossil steroids record the appearance of Demospongiae during the Cryogenian period. *Nature* 457: 718–721.
- Maldonado, M. and M. Dunfort, D.A. McCarthy, and C.M. Young. 2003. The cellular basis of photobehavior in the tufted parenchymella larva of demosponges. *Mar. Biol.* 143: 427–441.
- Maldonado, M. 2004. Choanoflagellates, choanocytes, and animal multicellularity. *Invertebr. Biol.* 123: 1–22.
- Martin, V.J. 1992. Characterization of RFamide-positive subset of ganglionic cells in the hydrozoan planular nerve net. *Cell Tissue Res.* 269: 431–438.
- Martin, V.J. 2002. Photoreceptors of cnidarians. *Can. J. Zool.* 80: 1703–1722.
- Matus, D.Q. and K. Pang, H. Marlow, C.W. Dunn, G.H. Thomsen, and M.Q. Martindale. 2006. Molecular evidence for deep evolutionary roots of bilaterality in animal development. *Proc. Natl. Acad. Sci. USA* 103: 11195–11200.
- Matus D.Q. and K. Pang, M. Daly, and M.Q. Martindale. 2007. Expression of Pax gene family members in the anthozoan cnidarian, *Nematostella vectensis*. *Evol. Dev.* 9: 25–38.

- McIver, S.B. Mechanoreception. pp. 71–132. *In*: G.A. Kerkut and L.I. Gilbert. [eds.] 1985. *Comprehensive Insect Physiology, Biochemistry, and Pharmacology*. Pergamon, Oxford.
- Medina, M. and A.G. Collins, J.D. Silberman, and M.L. Sogin. 2001. Evaluating hypotheses of basal animal phylogeny using complete sequences of large and small subunit rRNA. *Proc. Natl. Acad. Sci. USA* 98: 9707–9712.
- Mooi, R. and B. David, and G.A. Wray. 2005. Arrays in rays: terminal addition in echinoderms and its correlation with gene expression. *Evol. Dev.* 7: 542–555.
- Nakanishi, N. et al. 2008. Early development, pattern, and reorganization of the planula nervous system in Aurelia (Cnidaria, Scyphozoa). *Develop. Genes and Evol.* 218: 511.
- Nichols, S.A. and W. Dirks, J.S. Pearse, and N. King. 2006. Early evolution of animal cell signaling and adhesion genes. *PNAS* 103: 12451–12456.
- Niwa, N. et al. 2004. A conserved developmental program for sensory organ formation in *Drosophila melanogaster*. *Nat. Genet.* 36: 293–297.
- North, R.A. and A. Verkhatsky. 2006. Purinergic transmission in the central nervous system. *Pflugers Arch-Eur. J. Physiol.* 452: 479–485.
- O'Brien, E.K. and B.M. Degnan. 2003. Expression of Pax258 in the gastropod statocyst: insights into the antiquity of metazoan geosensory organs. *Evol. Dev.* 5: 572–578.
- Pan, L. and Z.Y. Yang, L. Feng, and L. Gan. 2005. Functional equivalence of Brn3 POU-domain transcription factors in mouse retinal neurogenesis. *Development* 132: 703–712.
- Piatigorsky, J. and Z. Kozmik. 2004. Cubozoan jellyfish: an Evo/Devo model for eyes and other sensory systems. *Int. J. Dev. Biol.* 48: 719–729.
- Plaza, S. 2001. Molecular basis for the inhibition of *Drosophila* eye development by Antennapedia. *The EMBO J.* 20: 802–811.
- Purschke, G. 2005. Sense organs in polychaetes (Annelida). *Hydrobiologia* 535/536: 53–78.
- Reinhardt, B. et al. 2004. HyBMP5-8b, a BMP5-8 orthologue, acts during axial patterning and tentacle formation in hydra. *Develop. Biol.* 267: 43–59.
- Richards, G.S. et al. 2008. Sponge genes provide new insight into the evolutionary origin of the neurogenic circuit. *Curr. Biol.* 18: 1156–1161.
- Römpler, H. et al. 2007. G Protein-coupled time travel: evolutionary aspects of GPCR research. *Mol. Interv.* 7: 17–25.
- Ruiz-Trillo, I. and A.J. Roger, G. Burger, M.W. Gray, and B.F. Lang. 2008. A phylogenomic investigation into the origin of Metazoa. *Mol. Biol. Evol.* 25: 664–672.
- Russell, F.S. 1970. *The Medusae of the British Isles*. Vol. 2. Cambridge University Press, Cambridge.
- Ryan, J.F. et al. 2006. The cnidarian-bilaterian ancestor possessed at least 56 homeoboxes: evidence from the starlet sea anemone, *Nematostella vectensis*. *GenomeBiology.com*, 7: R64.
- Sakarya, O. and K.A. Armstrong, M. Adamska, M. Adamski, I-F. Wang, B. Tidor, B.M. Degnan, T.H. Oakley, and K.S. Kosick. 2007. A post-synaptic scaffold at the origin of the animal kingdom. *PloS ONE* 2: e506.
- Salvini-Plawen, L.V. and E. Mayr. 1977. On the evolution of photoreceptors and eyes. *Evol. Biol.* 10: 207–263.
- Schlosser, G. 2007. How old genes make a new head: redeployment of Six and Eya genes during the evolution of vertebrate cranial placodes. *Integr. Comp. Biol.* 47: 343–359.
- Schlosser, G. 2006. Induction and specification of cranial placodes. *Dev. Biol.* 294: 303–351.
- Schierwater, B. and D. de Jong, and R. DeSalle. 2009. Placozoa and the evolution of Metazoa and intrasomatic cell differentiation. *Int. J. Biochem. Cell Biol.* 41: 370–379.
- Schierwater, B. and K. Kamm, M. Srivastava, D. Rokhsar, R.D. Rosengarten, and S.L. Dellaporta. 2008. The early ANTP gene repertoire: insights from the placozoan genome. *PloS ONE*, 3: e2457.
- Schneuwly, S. 1987. Redesigning the body plan of *Drosophila* by ectopic expression of the homoeotic gene *Antennapedia*. *Nature* 325: 816–818.

- Seipel, K. and N. Yanze, and V. Schmid. 2004. Developmental and evolutionary aspects of the basic helix-loop-helix transcription factors *Atonal-like 1* and *Achaete-scute homolog 2* in the jellyfish. *Dev. Biol.* 269: 331–345.
- Signorovitch, A.Y. and L.W. Buss, and S.L. Dellaporta. 2007. Comparative Genomics of Large Mitochondriain Placozoans. *PLOS Genetics* 3: e13.
- Simionato, E. et al. 2007. Origin and diversification of the basic helix-loop-helix gene family in metazoans: insights from comparative genomics. *BMC Evol. Biol.* 7: 33.
- Shubin, N. and C. Tabin, and S. Carroll. 1997. Fossils, genes and the evolution of animal limbs. *Nature* 388: 639–648.
- Smith, K.M. and L. Gee, and H.R. Bode. 2000. HyAlx, an aristaless-related gene, is involved in tentacle formation in *hydra*. *Development* 127: 4743–4752.
- Spangenberg, D.B. and E. Coccaro, R. Schwarte, and B. Lowe. 1996. Touch-plate and statolith formation in graviceptors of ephyrae which developed while weightless in space. *Scan. Micro.* 10: 875–888.
- Sperling, E.A. and D. Pisani, and K.J. Peterson. 2007. Poriferan paraphyly and its implications for Precambrian paleobiology. *Geol. Soc. Lond. Spec. Publ.* 286: 355–367.
- Srivastava, M. et al. 2008. The Trichoplax genome and the nature of placozoans. *Nature* 454: 955–960.
- Stierwald, M. and N. Yanze, R.P. Bamert, L. Kammermeier, and V. Schmid. 2004. The *Sine oculis*/Six class family of homeobox genes in jellyfish with and without eyes: development and eye regeneration. *Dev. Biol.* 274: 70–81.
- Suga, H. et al. 2008. Evolution and functional diversity of jellyfish opsins. *Curr. Biol.* 18: 51–55.
- Todi, S.V. and Y. Sharma, and D.F. Eberl. 2004. Anatomical and molecular design of the *Drosophila* antenna as a flagellar auditory organ. *Microsc. Res. Techniq.* 63: 388–399.
- Verger-Bocquet, M. 1981. Etude comparative, au niveau infrastructural, entre l'Œil de souche et les taches oculaires du stolon chez *Syllis spongicola* Grube (Annélide Polychète). *Archives de Zoologie Expérimentale et Générale* 122: 253–258.
- Vosshall, L.B. and H. Amrein, P.S. Morozov, A. Rzhetsky, and R. Axel. 1999. A spatial map of olfactory receptor expression in the *Drosophila* antenna. *Cell* 96: 725–736.
- Westfall, J.A. 2004. Neural pathways and innervation of cnidocytes in tentacles of sea anemones. *Hydrobiologia* 530/531: 117–121.
- Willenz, P. and G. Van De Vwer. 1986. Ultrastructural evidence of extruding exocytosis of residual bodies in the freshwater sponge *Ephydatia*. *J. Morphol.* 190: 307–318.
- Yahel, G. and D.I. Eerkes-Medrano, and S.P. Leys. 2006. Size independent selective filtration of ultraplankton by hexactinellid glass sponges. *Aquat. Microb. Ecol.* 45: 181–194.
- Yahel, G. et al. 2007. *In situ* feeding and metabolism of glass sponges (Hexactinellida, Porifera) studied in a deep temperate fjord with a remotely operated submersible. *Limnol. Oceanogr.* 52: 428.
- Yang, Q. and A.N. Bermingham, M.J. Finegold, and H.Y. Zoghbi. 2001. Requirement of *Math1* for secretory cell lineage commitment in the mouse intestine. *Science* 294: 2155–2158.
- Zacharuk, R.Y. 1980. Ultrastructure and function of insect Chemosensilla. *Ann. Rev. Entomol.* 25: 27–47.