

Hormonal signaling in cnidarians: do we understand the pathways well enough to know whether they are being disrupted?

Ann M. Tarrant

Accepted: 4 October 2006 / Published online: 18 January 2007
© Springer Science+Business Media, LLC 2007

Abstract Cnidarians occupy a key evolutionary position as basal metazoans and are ecologically important as predators, prey and structure-builders. Bioregulatory molecules (e.g., amines, peptides and steroids) have been identified in cnidarians, but cnidarian signaling pathways remain poorly characterized. Cnidarians, especially hydras, are regularly used in toxicity testing, but few studies have used cnidarians in explicit testing for signal disruption. Sublethal endpoints developed in cnidarians include budding, regeneration, gametogenesis, mucus production and larval metamorphosis. Cnidarian genomic databases, microarrays and other molecular tools are increasingly facilitating mechanistic investigation of signaling pathways and signal disruption. Elucidation of cnidarian signaling processes in a comparative context can provide insight into the evolution and diversification of metazoan bioregulation. Characterizing signaling and signal disruption in cnidarians may also provide unique opportunities for evaluating risk to valuable marine resources, such as coral reefs.

Keywords Bioregulation · Cnidaria · Coral · Endocrine · Signal disruption

Introduction

Hormonal signaling in cnidarians has not been fully characterized on either a molecular or a biochemical

level, and the potential for signal disruption is largely unknown. This review considers the state of knowledge on hormonal signaling, chemical bioregulation and signal disruption in cnidarians, focusing particularly on advances since the publication of the results of the Endocrine Disruption in Invertebrates: Endocrinology, Testing and Assessment workshop (deFur et al. 1999).

Why cnidarians: diversity, evolutionary significance and ecological role

The phylum Cnidaria contains four extant classes, the Hydrozoa (e.g., hydras), Scyphozoa (“true” jellyfishes), Cubozoa (box jellies) and Anthozoa (e.g., corals and anemones). The number of cnidarian species has not been rigorously assessed, but is estimated to be around 10,000 (Brusca and Brusca 1990). A definitive cnidarian species inventory is currently being established (D.G. Fautin, personal communication, December 30, 2005), and progress to date indicates that the subclass Hexacorallia (that includes anemones and corals) alone contains 2,899 valid species (Fautin 2005).

Cnidarians are usually classified as basal metazoans that form a sister group to the bilaterians, although these ancient evolutionary relationships are a subject of active research (Holland 1998; Gröger and Schmid 2001; Martindale 2005; Rokas et al. 2005). Because of their basal position and simple organization, it is sometimes assumed that bioregulation of cnidarian physiology must also be simple and that vertebrate features absent from model protostomes (e.g., nematodes and insects) are likely to have evolved after the divergence of the protostomes and the deuterostomes. Somewhat surprisingly, a comparative study indicated

A. M. Tarrant (✉)
Woods Hole Oceanographic Institution, Mailstop 32,
Woods Hole, MA 02543, USA
e-mail: atarrant@whoi.edu

that more than 10% of genes shared between cnidarians and humans have apparently been lost from model protostomes (Kortschak et al. 2003). Thus, it is not possible to use conserved features between vertebrates and model invertebrates alone to predict the complexity of cnidarian signaling processes (Miller et al. 2005; Technau et al. 2005). Further, elucidation of cnidarian signaling processes in a comparative context can provide insight into the evolution and diversification of metazoan bioregulation.

In addition to their key evolutionary position, cnidarians are also important as both predators and prey in aquatic ecosystems. Gelatinous cnidarians serve as prey for diverse taxa including other cnidarians, fishes and turtles. While gelatinous cnidarians are sometimes regarded as relatively unpalatable or of low nutritional value (e.g., Avent et al. 2001), cnidarians may be widely underestimated as prey sources because they tend to be rapidly digested (Arai et al. 2003; Arai 2005). As predators, cnidarians can dramatically change the composition of plankton and may impair fisheries yield through dietary overlap and direct predation (Arai 1988; Purcell and Arai 2001; Purcell and Sturdevant 2001). As an example, the hydroid, *Clytia gracilis*, can remove up to 40% of copepod nauplii daily production in a region of the Georges Bank (Atlantic coast of the United States, Madin et al. 1996). Copepod nauplii are a primary food source for larval cod and haddock, so hydroids can significantly reduce food availability and may also prey directly on the larval fish (Madin et al. 1996). Suspension-feeding benthic cnidarians also impact planktonic composition and may play an important role in benthic–pelagic coupling. For example, a Mediterranean gorgonian was found to consume large numbers of eggs and invertebrate larvae, particularly larval bivalves, with unknown effects on bivalve recruitment and population dynamics (Rossi et al. 2004).

Jellyfish (medusae, which may be hydrozoan, scyphozoan or cubozoan) aggregations or blooms are common episodic events, and the frequency and extent of blooms may be increasing (Mills 2001). Jellyfish blooms can have major ecological consequences. For example, an exotic jellyfish recently accounted for 98% of total fisheries sampling in the Yangtze estuary in China (summarized by Xian et al. 2005). Jellyfish blooms are caused and maintained by a combination of physical and poorly understood behavioral and physiological processes (Lotan et al. 1994; Purcell et al. 2000; Graham et al. 2001; Lucas 2001). Jellyfish blooms may also be aggravated by anthropogenic factors (Mills 2001) including overfishing of competitors (Brodeur et al. 2002), eutrophication and changes in estuarine

circulation (Xian et al. 2005). The role of hormonal or pheromonal signals in regulating jellyfish blooms is unknown. Similarly, it is unknown whether environmental chemicals affect jellyfish signaling and bloom dynamics.

Cnidarians also provide three-dimensional structure to benthic ecosystems, most notably tropical coral reefs. Reef ecosystems provide habitat for diverse taxa, protect shorelines and provide commercial and recreational resources for humans. Scleractinian coral biology is of particular interest due to the importance of corals in maintaining tropical reefs and increasing human concerns about reef degradation (Gardner et al. 2003; Hughes et al. 2003; Pandolfi et al. 2003). The chemical signals that regulate coral gametogenesis and spawning are poorly understood, and it is unknown whether environmental chemicals may disrupt these signals.

Routes of exposure

Cnidarians may be exposed to chemicals through uptake of dissolved compounds, ingestion of food particles, or contact with suspended solids and sediments. The relative importance of these routes of exposure varies with life history parameters, particularly habitat and mode of nutrition. Adult cnidarians may be benthic or pelagic, cnidarian gametes may be brooded or spawned, and larvae spend varying times (hours to months) in the water column. Cnidarians may be entirely carnivorous or may contain algal symbionts that fill some or all of their energetic needs. Exposure of scleractinian corals to chemicals is of particular concern because reef ecosystems are often located near highly populated coasts and may be exposed to contaminants through riverine input, sewage effluent, run-off, groundwater discharge, marine activities and spills (reviewed by Peters et al. 1997).

Cnidarians can take up dissolved chemicals through diffusion. The freshwater *Hydra* spp. are commonly used (Blaise and Kusui 1997; Holdway et al. 2001; Pascoe et al. 2003) and other cnidarians are occasionally used (e.g., anemones Mercier et al. 1997; colonial hydroids Chicu et al. 2000) in toxicity testing with dissolved contaminants. One explanation for the observed sensitivity of hydras to a range of chemicals is their diploblastic organization, which allows all cells potentially to be exposed to the surrounding medium and associated contaminants (Ingersoll et al. 1999). Similarly, Peters et al. (1997) suggested that reef-building corals might be particularly sensitive to lipophilic contaminants because corals typically

possess thin lipid-rich tissues, facilitating direct uptake. Incubations with radiolabeled compounds have demonstrated that corals can remove estrogens (Tarrant et al. 2001), petroleum hydrocarbons (Solbakken et al. 1984), and benzo [a]pyrene (Kennedy et al. 1992) from the surrounding seawater.

Few studies have examined the bioavailability of particle-associated contaminants to cnidarians. Harter and Matthews (2005) suggested that the burrowing anemone *Nematostella vectensis* could be used in sediment toxicity testing. Mayer et al. (2001) compared liquid removed from the oral cavity of a sea anemone with other invertebrate digestive fluids for their capacity to solubilize radiolabeled benzo[a]pyrene and zinc. They concluded that the material extracted from the anemone had a low ability to solubilize sediment-associated contaminants, but the method of sampling may not have accurately reflected the actual capacity of the anemone to solubilize contaminants. For example, particles may stick to the mucus-lined interior of the oral cavity and be subject to enzymatic activity.

Cnidarians may also be exposed to contaminants through ingestion of prey, although few studies have tested the effects of dietary exposures. For example, aqueous or dietary exposure of sea anemones to tributyltin (TBT) can affect zooxanthallae abundance, associated bacteria, and nematocyst discharge (Mercier et al. 1997). While this study was relatively unique in comparing an aqueous and a dietary exposure, only a single concentration was tested in each case and accumulation of TBT in the anemones was not measured. Clearly additional quantitative studies are needed to test the relative importance of different routes of chemical exposure to cnidarians.

In addition to directly affecting cnidarians, chemicals may also accumulate in cnidarian tissues, where they may affect cnidarian predators. Cnidarian tissues can be very lipid rich (Stimson 1987), allowing for rapid uptake and storage of lipophilic contaminants. For example, high levels of PCBs were measured in tissues of a soft coral from Guam, relative to other invertebrates. Tissue accumulation of PCBs may be due in part to the high tissue concentration of triglycerides and other lipids (Denton et al. 2006). While uptake of lipophilic chemicals by cnidarians may be rapid, metabolism and elimination often proceeds slowly (Solbakken et al. 1984; Kennedy et al. 1992; Peters et al. 1997), possibly due to low activity of xenobiotic metabolizing enzymes (Gassman and Kennedy 1992). The tissue lipid concentration of some corals decreases following the release of eggs or larvae (Stimson 1987); however, additional study is needed to

determine whether accumulated lipophilic contaminants are mobilized during spawning events. In addition to organic chemicals, heavy metals can also accumulate in cnidarian tissues (Mitchelmore et al. 2003) and can be transferred up the food chain. For example, high levels of cadmium and other metals in leatherback turtles are thought to be derived from their jellyfish prey (Caurant et al. 1999).

Hormonal signaling in cnidarians

In classical endocrinology, hormones are synthesized by endocrine organs, secreted into the bloodstream and transported to target tissues where they bind to specific receptors. Cnidarian cells are differentiated into tissues but not into specialized endocrine organs, and circulation occurs primarily through diffusion. While the term “endocrinology” is not strictly applicable to cnidarians, this discussion may be extended to include physiological regulation controlled by bioactive signal molecules (e.g., secondary messengers, neurotransmitters and hormones) synthesized within the organism. This section will briefly describe cnidarian hormones and neuropeptides and recent discoveries in cnidarian signaling. For a more extensive discussion of the cnidarian bioregulation, readers can consult several recent reviews (Leitz 2001; Grimmelikhuijzen et al. 2002; Müller and Leitz 2002; Tarrant 2005).

Cnidarians are among the simplest animals to possess a nervous system. The cnidarian nervous system has been described as a “nerve net” but may also contain nerve rings and other areas of centralization (Grimmelikhuijzen 1985). Cnidarians synthesize monoamines that act as neurotransmitters in other animals including catecholamines and indolamines (Pani and Anctil 1994; Leitz 2001). Indolamines, such as serotonin, may act as neurohormones in some cnidarians. In the sea pansy, *Renilla koellikeri*, serotonin stimulates rhythmic muscular contraction (Anctil 1989) and spawning (Tremblay et al. 2004). Seasonal peaks in melatonin coincided with the first stages of sexual maturation (Mechawar and Anctil 1997). Serotonin can also experimentally induce metamorphosis of hydrozoan larvae (McCauley 1997; Walther and Fleck 1998). Specific binding sites have been identified in cnidarians for serotonin (Hajj-Ali and Anctil 1997), β -Adrenergic agonists (Awad and Anctil 1993) and γ -aminobutyric acid (Pierobon et al. 1995). Also, genes for G protein-coupled receptors have been cloned (Nothacker and Grimmelikhuijzen 1993; New et al. 2000; Bouchard et al. 2003), but the ligands for these

receptors have not yet been identified. One G protein-coupled receptor is phylogenetically related to dopamine and adrenergic receptors but not responsive to known biogenic amines (Bouchard et al. 2003, 2004).

The majority of signaling molecules known in cnidarians are peptides that may act as neurotransmitters and/or neurohormones. Neuropeptides have been extensively studied as regulators of hydrozoan development and metamorphosis, and hundreds of peptides are systematically being purified, sequenced and screened from *Hydra magnipapillata* (Takahashi et al. 1997). The “head activator” peptide, first purified and sequenced from *Hydra attenuata* and *Anthopleura elegantissima* is a potent morphogen that triggers neurogenesis and head-specific growth (Schaller and Bodenmüller 1981). Immunoreactive gonadotropin-releasing hormone has been detected in cnidarians and may help to regulate gametogenesis and spawning (Anctil 2000; Twan et al. 2006). Peptides are roughly classified into families based on the amino acid sequence of the C-terminus (e.g., [G]LW-amides and RF-amides), and in some cases peptides with a similar C-terminus seem to have similar biological activity (Leitz 2001). LW-amides, including “metamorphosin A” stimulate contraction of some cnidarian muscles and trigger metamorphosis of hydrozoan planulae (Leitz et al. 1994; Takahashi et al. 1997; Plickert et al. 2003). While their role in cnidarian physiology has not been fully elucidated, LW-amides have been hypothesized to function in tentacle formation, metamorphosis and larval physiology (McFadden and Spencer 1991; Brumwell and Martin 1996). RF-amides affect cnidarian muscle contraction, feeding responses and exfoliation of gamete follicles (McFarlane and Grimmelikhuijzen 1991; Pierobon et al. 1997b; Tremblay et al. 2004). The receptors for these peptides have not been identified, but genes encoding preprohormones have been sequenced from several species (Levieu et al. 1997; Darmer et al. 1998).

Vertebrate-type sex steroids have been detected by immunoassay in several anthozoans, and concentrations vary seasonally and between sexes (Slattery et al. 1999; Tarrant et al. 1999; Pernet and Anctil 2002; Twan et al. 2003). Most notably, estrogen concentrations were elevated in tissues of the coral *Euphyllia ancora* (Twan et al. 2003) and the sea pansy *Renilla koellikeri* (Pernet and Anctil 2002) prior to spawning, and testosterone concentration in the soft coral *Sinularia polydactyla* decreased following spawning (Slattery et al. 1997). Estradiol is released into the water column in association with anthozoan spawning (Atkinson and Atkinson 1992; Slattery et al. 1999; Twan et al. 2003). Together these observations prompted speculation that

free or conjugated estrogens might serve as chemical cues or pheromones to stimulate coral spawning, but the source of sex steroids in cnidarian tissues has not been demonstrated. Low levels of estrogen synthesis from androgen substrates by coral homogenates has been reported in one study (Twan et al. 2003), but other studies have not detected estrogen synthesis (Slattery et al. 1997; Tarrant et al. 2003). The mechanism of steroid hormone action in cnidarian tissues is also unknown. While steroid receptors have not been identified in any cnidarian, several cnidarian nuclear receptor genes have been identified, including homologs to COUP-TF (chicken ovalbumin upstream promoter transcription factor, Escriva et al. 1997; Grasso et al. 2001; A.M. Tarrant, unpublished data) and RXR (retinoic acid “x” receptor, Kostrouch et al. 1998). Some cnidarian nuclear receptors are sufficiently divergent from vertebrate sequences that they cannot easily be assigned to a nuclear receptor subfamily or a clear vertebrate homolog (Grasso et al. 2001). Because a classical estrogen receptor has not been identified in any cnidarian, estrogens or other steroids may act through a “functional estrogen receptor” that does not belong to the steroid receptor protein family described in vertebrates.

Overall, hormonal signaling and bioregulatory pathways are still largely uncharacterized in cnidarians. Considerable progress has been made in identifying bioactive molecules, particularly peptides, but in most cases their receptors have not been identified and their precise physiological function is unknown. Other classes of signaling molecules such as fatty acids and eicosanoids may also act as cnidarian hormones (Coll et al. 1994, 1995; Pierobon et al. 1997a, b), but more research is needed to identify the functions of these compounds and their mechanisms of action. Iodinated organic molecules, such as thyroxine, have been proposed to hormonally regulate strobilation and metamorphosis in the scyphozoan jellyfish *Aurelia aurita* (Spangenberg 1971). A recent study indicates that this physiological response is actually induced by iodine, which is formed through oxidation of iodide (Berking et al. 2005). The authors concluded that thyroxine is a waste product in this pathway that later developed as a vertebrate metabolic hormone.

Endocrine disruption in cnidarians

Endocrine disruption has not been documented in cnidarians, which is not surprising given that cnidarian hormonal signaling pathways are poorly characterized and few appropriate endpoints have been established.

A few studies have tested the effects of estrogenic compounds on cnidarians. *Montipora capitata* coral colonies treated with exogenous estradiol (nominally $2.3 \mu\text{g L}^{-1}$) for 3 weeks prior to spawning released fewer (29%) egg-sperm bundles than control colonies (Tarrant et al. 2004). *Porites compressa* coral fragments exposed continuously to 2 ng L^{-1} estrone for 2–8 weeks had lower (13–24%) skeletal growth rates than controls (Tarrant et al. 2004). On the other hand, when *Hydra vulgaris* was exposed to ethinyl estradiol and bisphenol A, both of which are estrogenic in vertebrates, adverse physiological effects were only seen at high doses ($40 \mu\text{g L}^{-1}$) (Pascoe et al. 2002). Bisphenol A also impaired sexual and asexual reproduction in *Hydra oligactis*, but the authors concluded that the adverse effects were most likely due to general toxicity of the compound (Fukuhori et al. 2005).

Cnidarians, particularly hydras, are widely used in toxicity testing and in teratogenicity testing of pharmaceuticals. Several compounds that disrupt endocrine signaling in other animals have been tested for toxicity or disruptive activity in cnidarians. For example, reef-building corals are affected by herbicides such as atrazine and diuron, but the primary effects seem to be direct toxicity to photosystem II of the symbiotic algae within the coral tissues (reviewed by Jones 2005). Cnidarians are sensitive to metals, including cadmium, zinc and butyltin (Chicu and Berking 1997; Mercier et al. 1997; Holdway et al. 2001; Harter and Matthews 2005), although reproductive abnormalities comparable to the imposex phenomenon observed in gastropods have not been noted.

Toxic effects of petroleum products and dispersants have also been observed, particularly on coral larval metamorphosis (Epstein et al. 2000; Negri and Heyward 2000). A suite of organic compounds, including hydrocarbons and TBT, antagonize induced metamorphosis in the colonial hydroid *Hydractinia echinata*. Structure–activity relationships have been determined for several classes of compounds with respect to their effect on *H. echinata* metamorphosis (Chicu and Berking 1997; Chicu et al. 2000). Generally, and particularly within a class of compounds, inhibition of metamorphosis increases with increasing octanol/water partition coefficient (i.e., more lipophilic compounds are more inhibitory).

As described in the previous section, considerable progress has been made recently toward identifying bioregulatory molecules, especially peptides that regulate metamorphosis. A mechanistic understanding of signaling processes in cnidarians will allow for monitoring of signal disruption and for a better distinction between general toxicity and signal disruption.

Test species and endpoints

While few studies have explicitly tested for disruption of hormonal signaling, several cnidarian taxa have been used recently in toxicity testing, including hydras, colonial hydroids, sea anemones, and scleractinian corals. In general, the relative sensitivity of different cnidarians to chemicals has not been assessed. One comparative study demonstrated that *H. vulgaris* is more sensitive to cadmium and zinc toxicity than *Hydra viridissima* (Holdway et al. 2001).

Hydras have been the cnidarians most widely used in toxicity testing (Blaise and Kusui 1997; Holdway et al. 2001; Pascoe et al. 2003). While toxicity testing with hydras has not been standardized, the most common sublethal endpoints are budding, polyp structure and polyp regeneration. Most laboratory strains of hydras reproduce primarily by budding, but sexually reproducing strains have been used to test the effects of chemicals on gametogenesis (Segner et al. 2003; Fukuhori et al. 2005). *H. vulgaris* was selected as the cnidarian test species in the European IDEA project, which investigated effects of environmental estrogens on diverse invertebrates (Segner et al. 2003). As test species, hydras have the advantages of rapid growth, small size, ease of culture, and the availability of clonal strains. In addition, the *H. magnipapillata* genome is being sequenced, and a wealth of information is available regarding hydra development, neurobiology and toxicology. One disadvantage of using hydras to screen for disruption of cnidarian signaling is that hydras are highly derived freshwater animals and not necessarily representative of the predominantly marine, more “typical” cnidarians.

In addition to solitary hydras, colonial marine hydrozoans in the genus *Hydractinia* are widely used in studies of development, metamorphosis and immune response (reviewed by Frank et al. 2001). *Hydractinia* spp. have been particularly useful in mechanistic studies linking an environmental stimulus [compound(s) derived from bacterial films] with a signaling cascade resulting in metamorphosis (reviewed by Müller and Leitz 2002). While *Hydractinia* spp. share many advantages with hydras and have been used to evaluate the effects of some chemicals (Leitz and Wirth 1991), they have not been fully exploited as a model for investigation of toxicity and signal disruption by environmental contaminants.

Anemones have not been used extensively in toxicity testing to date but may be used more extensively in the future. The small burrowing anemone, *N. vectensis*, is easy to maintain, matures rapidly, and spawns predictably in the laboratory (Darling et al. 2005).

The *N. vectensis* genome has been sequenced and assembled (Sullivan et al. 2006), and characterization of *N. vectensis* genes has already provided significant insight into the evolution of animal development. *N. vectensis* has a wide geographic range, including large portions of the Pacific and Atlantic coasts of North America and the Southeastern coast of England. *N. vectensis* is most common on the Atlantic coast of the United States, where it inhabits a range of estuarine habitats and may be useful as an ecotoxicological model. Harter and Matthews (2005) exposed *N. vectensis* to acute and chronic doses of cadmium chloride and measured mortality, change in weight, and egg production. They found that the sensitivity of *N. vectensis* to cadmium is similar to the sensitivity of other invertebrates and suggested that *N. vectensis* could be further developed as a test organism for dissolved and sediment-associated toxicity testing. Other anemones have been used in toxicity testing; for example, exposure of *Aiptasia pallida* to TBT resulted in changes in mucus secretion and abundance of symbionts, bacterial aggregates and undischarged nematocysts (Mercier et al. 1997).

Scleractinian corals have been recently used to evaluate the effects of chemicals including herbicides, petroleum products, dispersants and estrone (Epstein et al. 2000; Negri and Heyward 2000; Tarrant et al. 2004; Jones 2005). Endpoints measured included tissue thickness, skeletal growth, fecundity, fertilization, and larval metamorphosis. As test species, scleractinian corals have clear ecological relevance but are not easily accessible to many laboratories due to geographic constraints and legal protections. Relative to hydras or *Nematostella*, corals are difficult to maintain in the laboratory and generally take several years to reach reproductive maturity. Analysis of reproductive endpoints is further limited by the seasonal reproductive cycle of many corals.

Molecular tools such as cDNA arrays (Edge et al. 2005; Morgan et al. 2005) and the ELISA-based “Cellular Diagnostics” (which measures concentrations of proteins associated with detoxification and stress responses, Downs et al. 2005) have been developed for corals and may be used to evaluate the effects of chemicals. Differential display has been effectively used to screen for bioactivity of peptides in hydras (Takahashi et al. 1997), and this approach could be adapted to screen for signal disruption. Collectively, these techniques can provide molecular or biochemical endpoints for chemical effects on cnidarian physiology, including disruption of signaling pathways.

The future of cnidarians as indicators of endocrine disruptive chemicals

Given the limited knowledge of cnidarian signaling pathways and the few studies of signal disruption, cnidarians currently have limited use as models for evaluating signal disruption. On the other hand, cnidarians are sensitive to many stressors and have been used as indicators of water quality. Thus, with a better understanding of regulatory processes and development of appropriate endpoints, cnidarians may become valuable indicators of exposure to disruptive chemicals and other stressors. In many cases, cnidarians are subjected to multiple stressors, which complicates the detection of signal disruption by environmental contaminants in the field. For example, in coastal environments, cnidarians and other organisms may simultaneously be exposed to increased sedimentation, eutrophication, bacterial loads and mixtures of potentially disruptive chemicals. Without a mechanistic understanding of cnidarian regulatory pathways, it will be extremely difficult to separate signal disruption from other stresses. Ongoing studies, facilitated by the release of genomic sequences and the development of molecular tools will provide a more complete context for evaluating disruption of cnidarian signaling.

References

- Ancil M (1989) Modulation of rhythmic contraction by serotonin via cyclic AMP in the coelenterate *Renilla koelikeri*. *J Comp Physiol* 159:491–500
- Ancil M (2000) Evidence for gonadotropin-releasing hormone-like peptides in a cnidarian nervous system. *Gen Comp Endocrinol* 199:317–328
- Arai MN (1988) Interactions of fish and pelagic coelenterates. *Can J Zool* 66:1913–1927
- Arai MN (2005) Predation on pelagic coelenterates: a review. *J Mar Biol Assoc UK* 85:523–536
- Arai MN, Welch DW, Dunsmuir AL, Jacobs MC, Ladouceur AR (2003) Digestion of pelagic Ctenophora and Cnidaria by fish. *Can J Fish Aquat Sci* 60:825–829
- Atkinson S, Atkinson MJ (1992) Detection of estradiol-17 β during a mass coral spawn. *Coral Reefs* 11:33–35
- Avent SR, Bollens SM, Butler M, Horgan E, Rountree R (2001) Planktonic hydroids on Georges Bank: ingestion and selection by predatory fishes. *Deep Sea Res Part II* 48:673–684
- Awad E, Ancil M (1993) Identification of beta-like adrenoceptors associated with bioluminescence in the sea pansy *Renilla koelikeri*. *J Exp Biol* 177:181–200
- Berking S, Czech N, Gerharz M, Herrmann K, Hoffmann U, Raifer H, Sekul G, Siefker B, Sommerei A, Vedder F (2005) A newly discovered oxidant defense system and its involvement in the development of *Aurelia aurita* (Scyphozoa, Cnidaria): reactive oxygen species and elemental iodine control medusa formation. *Int J Dev Biol* 49:969–976

- Blaise C, Kusui T (1997) Acute toxicity assessment of industrial effluents with a microplate-based *Hydra attenuata* assay. *Environ Toxicol Water Qual* 12:53–60
- Bouchard C, Ribeiro P, Dube F, Anctil M (2003) A new G protein-coupled receptor from a primitive metazoan shows homology with vertebrate aminergic receptors and displays constitutive activity in mammalian cells. *J Neurochem* 86:1149–1161
- Bouchard C, Ribeiro P, Dube F, Demers C, Anctil M (2004) Identification of a novel aminergic-like G protein-coupled receptor in the cnidarian *Renilla koellikeri*. *Gene* 341:67–75
- Brodeur RD, Sugisaki H, George L, Hunt J (2002) Increases in jellyfish biomass in the Bering Sea: implications for the ecosystem. *Mar Ecol Prog Ser* 233:89–103
- Brumwell G, Martin V (1996) Ultrastructural localization of RFamide-like peptides in neuronal dense-cored vesicles of a cnidarian planula larva. *Invert Biol* 115:13–19
- Brusca RC, Brusca GG (1990) *Invertebrates*. Sinauer Associates Inc., Sunderland, p 922
- Caurant F, Bustamante P, Bordes M, Miramand P (1999) Bioaccumulation of cadmium, copper and zinc in some tissues of three species of marine turtles stranded along the French Atlantic coasts. *Mar Pollut Bull* 38:1085–1091
- Chicu S, Berking S (1997) Interference with metamorphosis induction in the marine cnidaria *Hydractinia echinata* (Hydrozoa): a structure–activity relationship analysis of lower alcohols, aliphatic and aromatic hydrocarbons, thiophenes, tributyl tin and crude oil. *Chemosphere* 34:1851–1866
- Chicu S, Herrmann K, Berking S (2000) An approach to calculate the toxicity of simple organic molecules on the basis of QSAR analysis in *Hydractinia echinata* (Hydrozoa, Cnidaria). *Quant Struct Act Relat* 19:227–236
- Coll JC, Bowden BF, Meehan GV, Konig GM, Carroll AR, Tapiolas DM, Aliño PM, Heaton A, De Nys R, Leone PA, Maida M, Aceret TL, Willis RH, Babcock RC, Willis BL, Florian Z, Clayton MN, Miller RL (1994) Chemical aspects of mass spawning in corals. I. Sperm-attractant molecules in the eggs of the scleractinian coral *Montipora digitata*. *Mar Biol* 118:177–182
- Coll J, Leone P, Bowden B, Carroll A, Konig G, Heaton A, de Nys R, Maida M, Aliño P, Willis R, Babcock R, Florian Z, Clayton M, Miller R, Alderslade P (1995) Chemical aspects of mass spawning in corals. II. (-)-Epi-thunbergol, the sperm attractant in the eggs of the soft coral *Lobophytum crassum* (Cnidaria: Octocorallia). *Mar Biol* 123:137–143
- Darling J, Reitzel A, Burton P, Mazza M, Ryan J, Sullivan J, Finnerty J (2005) Rising starlet: the starlet sea anemone, *Nematostella vectensis*. *Bioessays* 27:211–221
- Darmer D, Hauser F, Nothacker H, Bosch T, Williamson M, Grimmelikhuijzen CJP (1998) Three different prohormones yield a variety of *Hydra*-RFamide (Arg-Phe-NH₂) neuropeptides in *Hydra magnipapillata*. *Biochem J* 332:403–412
- deFur PL, Crane M, Tattersfield LJ, Ingersoll CG (eds) (1999) *Endocrine disruption in invertebrates: endocrinology, testing, and assessment*. SETAC, Pensacola, Brussels, 320 p
- Denton GRW, Concepcion LP, Wood HR, Morrison RJ (2006) Polychlorinated biphenyls (PCBs) in marine organisms from four harbours in Guam. *Mar Pollut Bull* 52:711–718
- Downs C, Fauth J, Robinson C, Curry R, Lanzendorf B, Halas J, Halas J, Woodley C (2005) Cellular diagnostics and coral health: declining coral health in the Florida Keys. *Mar Pollut Bull* 51:558–569
- Edge S, Morgan M, Gleason D, Snell T (2005) Development of a coral cDNA array to examine gene expression profiles in *Montastrea faveolata* exposed to environmental stress. *Mar Pollut Bull* 51:507–523
- Epstein N, Bak R, Rinkevich B (2000) Toxicity of third generation dispersants and dispersed Egyptian crude oil on Red Sea coral larvae. *Mar Pollut Bull* 40:497–503
- Escriba H, Safi R, Hanni C, Langlois M-C, Saumitou-Laprade P, Stehelin D, Capron A, Pierce R, Laudet V (1997) Ligand binding was acquired during the evolution of nuclear receptors. *Proc Natl Acad Sci USA* 94:6803–6908
- Fautin DG (2005) Hexacorallians of the world. <http://hercules.kgs.ku.edu/hexacorall/anemone2/index.cfm>
- Frank U, Leitz T, Muller W (2001) The hydroid *Hydractinia*: a versatile, informative cnidarian representative. *Bioessays* 23:963–971
- Fukuhori N, Kitano M, Kimura H (2005) Toxic effects of bisphenol A on sexual and asexual reproduction in *Hydra oligactis*. *Arch Environ Contam Toxicol* 48:495–500
- Gardner TA, Côté IM, Gill JA, Grant A, Watkinson AR (2003) Long-term region-wide declines in Caribbean corals. *Science* 203:958–960
- Gassman NJ, Kennedy CJ (1992) Cytochrome P-450 content and xenobiotic metabolizing enzyme activities in the scleractinian coral, *Favia fragum* (Esper). *Bull Mar Sci* 50:320–330
- Graham W, Pages F, Hamner W (2001) A physical context for gelatinous zooplankton aggregations: a review. *Hydrobiologia* 451:199–212
- Grasso LC, Hayward DC, Trueman JWH, Hardie KM, Janssens PA, Ball EE (2001) The evolution of nuclear receptors: evidence from the coral *Acropora*. *Mol Phylogenet Evol* 21:93–102
- Grimmelikhuijzen CJP (1985) Antisera to the sequence Arg-Phe-amide visualize neuronal centralization in hydroid polyps. *Cell Tissue Res* 241:171–182
- Grimmelikhuijzen CJP, Williamson M, Hansen GN (2002) Neuropeptides in cnidarians. *Can J Zool* 80:1690–1702
- Gröger H, Schmid V (2001) Larval development in Cnidaria: a connection to Bilateria? *Genesis* 29:110–114
- Hajji-Ali I, Anctil M (1997) Characterization of a serotonin receptor in the cnidarian *Renilla koellikeri*: a radiobinding analysis. *Neurochem Int* 31:83–93
- Harter VL, Matthews RA (2005) Acute and chronic toxicity test methods for *Nematostella vectensis* Stephenson. *Bull Environ Contam Toxicol* 74:830–836
- Holdway D, Lok K, Semaan M (2001) The acute and chronic toxicity of cadmium and zinc to two hydra species. *Environ Toxicol* 16:557–565
- Holland P (1998) Major transitions in animal evolution: a developmental genetic perspective. *Am Zool* 38:829–842
- Hughes T, Baird A, Bellwood D, Card M, Connolly S, Folke C, Grosberg R, Hoegh-Guldberg O, Jackson J, Kypuros J, Lough J, Marshall P, Nystroem M, Palumbi S, Pandolfi J, Rosen B, Roughgarden J (2003) Climate change, human impacts, and the resilience of coral reefs. *Science* 301:929–933
- Ingersoll C, Hutchinson T, Crane M, Dodson S, DeWitt T, Gies A, Huet M-C, McKenny C Jr, Oberdörster E, Pascoe D, Versteeg D, Warwick O (1999) Laboratory toxicity tests for evaluating potential effects of endocrine-disrupting compounds. In: deFur PL, Crane M, Ingersoll CG, Tattersfield LJ (eds) *Endocrine disruption in invertebrates: endocrinology, testing and assessment*. SETAC, Pensacola, Brussels, pp 107–197
- Jones R (2005) The ecotoxicological effects of photosystem II herbicides on corals. *Mar Pollut Bull* 51:495–506
- Kennedy C, Gassman N, Walsh P (1992) The fate of benzo[a]pyrene in the scleractinian corals *Favia fragum* and *Montastrea annularis*. *Mar Biol* 113:313–318

- Kortschak RD, Samuel G, Saint R, Miller DJ (2003) EST analysis of the cnidarian *Acropora millepora* reveals extensive gene loss and rapid sequence divergence in model invertebrates. *Curr Biol* 14:R106–R108
- Kostrouch Z, Kostrouchova M, Love W, Jannini E, Piatigorsky J, Rall JE (1998) Retinoic acid X receptor in the diploblast, *Tripedalia cystophora*. *Proc Natl Acad Sci USA* 95:13442–13447
- Leitz T (2001) Endocrinology of the Cnidaria: state of the art. *Zool Anal Complex Syst* 103:202–221
- Leitz T, Wirth A (1991) Vanadate, known to interfere with signal transduction, induces metamorphosis in *Hydractinia* (Coelenterata: Hydrozoa) and causes profound alteration of the larval and postmetamorphic body pattern. *Differentiation* 47:119–127
- Leitz T, Morand K, Mann M (1994) Metamorphosin A, a novel peptide controlling development of the lower metazoan, *Hydractinia echinata*. *Dev Biol* 163:440–446
- Lievie I, Williamson M, Grimmelikhuijzen CJP (1997) Molecular cloning of a preprohormone from *Hydra magnipapillata* containing multiple copies of *Hydra*-LWamide (Leu-Trp-NH₂) neuropeptides: evidence for processing at Ser and Asn residues. *J Neurochem* 68:1319–1325
- Lotan A, Fine M, Ben-Hillel R (1994) Synchronization of the life cycle and dispersal pattern of the tropical invader scyphomedusan *Rhopilema nomadica* is temperature dependent. *Mar Ecol Prog Ser* 109:59–65
- Lucas C (2001) Reproduction and life history strategies of the common jellyfish, *Aurelia aurita*, in relation to its ambient environment. *Hydrobiologia* 451:229–246
- Madin LP, Bollens SM, Horgan E, Butler M, Runge J, Sullivan BK, Klein-MacPhee G, Durbin E, Durbin AG, Keuren DV, Plourde S, Bucklin A, Clarke ME (1996) Voracious planktonic hydroids: unexpected predatory impact on a coastal marine ecosystem. *Deep Sea Res Part II* 43:1823–1829
- Martindale MQ (2005) The evolution of metazoan axial properties. *Nat Rev Genet* 6:917–927
- Mayer LM, Weston DP, Bock MJ (2001) Benzo[a]pyrene and zinc solubilization by digestive fluids of benthic invertebrates—a cross-phyletic study. *Environ Toxicol Chem* 20:1890–1900
- McCauley D (1997) Serotonin plays an early role in the metamorphosis of the hydrozoan *Phialidium gregarium*. *Dev Biol* 190:229–240
- McFadden N, Spencer A (1991) The possible involvement of Arg-Phe-amide immunoreactive neurons during tentacle development and regeneration in the hydromedusa *Polyorchis penicillatus*. *Can J Zool* 70:567–577
- McFarlane I, Grimmelikhuijzen CJP (1991) Three anthozoan neuropeptides: Antho-RFamide and Antho-RWamides I and II, modulate spontaneous tentacle contractions in sea anemones. *J Exp Biol* 155:669–673
- Mechawar N, Anctil M (1997) Melatonin in a primitive metazoan: seasonal changes of levels and immunohistochemical visualization in neurons. *J Comp Neurol* 387:243–254
- Mercier A, Pelletier E, Hamel J-F (1997) Effects of butyltins on the symbiotic sea anemone *Aiptasia pallida* (Verrill). *J Exp Mar Biol Ecol* 215:289–304
- Miller DJ, Ball EE, Technau U (2005) Cnidarians and ancestral genetic complexity in the animal kingdom. *Trends Genet* 21:536–539
- Mills C (2001) Jellyfish blooms: are populations increasing globally in response to changing ocean conditions? *Hydrobiologia* 451:55–68
- Mitchelmore CL, Ringwood AH, Weis VM (2003) Differential accumulation of cadmium and changes in glutathione levels as a function of symbiotic state in the sea anemone *Anthopleura elegantissima*. *J Exp Mar Biol Ecol* 284:71–85
- Morgan M, Edge S, Snell T (2005) Profiling differential gene expression of corals along a transect of waters adjacent to the Bermuda municipal dump. *Mar Pollut Bull* 51:524–533
- Müller W, Leitz T (2002) Metamorphosis in the cnidaria. *Can J Zool* 80:1755–1771
- Negri A, Heyward A (2000) Inhibition of fertilization and larval metamorphosis of the coral *Acropora millepora* (Ehrenberg, 1834) by petroleum products. *Mar Pollut Bull* 41:420–427
- New D, Wong Y, Wong J (2000) Cloning of a novel G-protein-coupled receptor from the sea anemone nervous system. *Biochem Biophys Res Commun* 271:761–769
- Nothacker H-P, Grimmelikhuijzen CJP (1993) Molecular cloning of a novel, putative G protein-coupled receptor from sea anemones structurally related to members of the FSH, TSH, LH/CG receptor family from mammals. *Biochem Biophys Res Commun* 179:1062–1069
- Pandolfi JM, Bradbury RH, Sala E, Hughes TP, Bjorndal KA, Cooke RG, McArdle D, McClenachan L, Newman MJH, Paredes G, Warner RR, Jackson JBC (2003) Global trajectories of the long-term decline of coral reef ecosystems. *Science* 301:955–958
- Pani A, Anctil M (1994) Evidence for biosynthesis and catabolism of monoamines in the sea pansy *Renilla koellikeri* (Cnidaria). *Neurochem Int* 25:465–474
- Pascoe D, Carroll K, Karntanut W, Watts M (2002) Toxicity of 17 α -ethinylestradiol and bisphenol A to the freshwater cnidarian *Hydra vulgaris*. *Arch Environ Contam Toxicol* 43:56–63
- Pascoe D, Karntanut W, Müller CT (2003) Do pharmaceuticals affect freshwater invertebrates? A study with the cnidarian *Hydra vulgaris*. *Chemosphere* 51:521–528
- Pernet V, Anctil M (2002) Annual variations and sex-related differences of estradiol-17 β ?levels in the anthozoan *Renilla koellikeri*. *Gen Comp Endocrinol* 129:63–68
- Peters EC, Gassman NJ, Firman JC, Richmond RH, Power EA (1997) Ecotoxicology of tropical marine ecosystems. *Environ Toxicol Chem* 16:12–40
- Pierobon P, Concas A, Santoro G, Marino G, Minei R, Pannaccione A, Mostallino M, Biggio G (1995) Biochemical and functional identification of GABA receptors in *Hydra vulgaris*. *Life Sci* 56:1485–1497
- Pierobon P, De Petrocellis L, Minei R, Di Marzo V (1997a) Arachidonic acid and eicosanoids in Hydra: possible endogenous signals involved in chemoreception and modulation of the feeding behaviour. *Adv Exp Med Biol* 433:363–366
- Pierobon P, De Petrocellis L, Minei R, Di Marzo V (1997b) Arachidonic acid as an endogenous signal for the glutathione induced feeding response in *Hydra*. *Cell Mol Life Sci* 53:61–68
- Plickert G, Schetter E, Verhey-Van-Wijk N, Schloscherr J, Steinbuchel M, Gajewski M (2003) The role of alpha-amidated neuropeptides in hydroid development—LWamides and metamorphosis in *Hydractinia echinata*. *Int J Dev Biol* 47:439–450
- Purcell JE, Arai MN (2001) Interactions of pelagic cnidarians and ctenophores with fish: a review. *Hydrobiologia* 45:27–44
- Purcell JE, Sturdevant MV (2001) Prey selection and dietary overlap among zooplanktivorous jellyfish and juvenile fishes in Prince William Sound, Alaska. *Mar Ecol Prog Ser* 210:67–83

- Purcell J, Brown E, Stokesbury K, Haldorson L, Shirley T (2000) Aggregations of the jellyfish *Aurelia labiata*: abundance, distribution, association with age-0 walleye pollock, and behaviors promoting aggregation in Prince William Sound, Alaska, USA. *Mar Ecol Prog Ser* 195:145–158
- Rokas A, Kruger D, Carroll SB (2005) Animal evolution and the molecular signature of radiations compressed in time. *Science* 310:1933–1938
- Rossi S, Ribes M, Coma R, Gili J-M (2004) Temporal variability in zooplankton prey capture rate of the passive suspension feeder *Leptogorgia sarmentosa* (Cnidaria: Octocorallia), a case study. *Mar Biol* 144:89–99
- Schaller H, Bodenmüller H (1981) Isolation and amino acid sequence of a morphogenetic peptide from hydra. *Proc Natl Acad Sci USA* 78:7000–7004
- Segner H, Carroll K, Fenske M, Janssen C, Maack G, Pascoe D, Schäfers C, Vandenberg G, Watts M, Wenzel A (2003) Identification of endocrine-disrupting effects in aquatic vertebrates and invertebrates: report from the European IDEA project. *Ecotoxicol Environ Saf* 54:302–314
- Slattery M, Hines GA, Watts SA (1997) Steroid metabolism in Antarctic soft corals. *Polar Biol* 18:76–82
- Slattery M, Hines GA, Starmer J, Paul VJ (1999) Chemical signals in gametogenesis, spawning, and larval settlement and defense of the soft coral *Simularia polydactyla*. *Coral Reefs* 18:75–84
- Solbakken J, Knap A, Sleeter T, Searle C, Palmork K (1984) Investigation into the fate of ¹⁴C-labeled xenobiotics (naphthalene, phenanthrene, 2,4,5,2',2',5'-hexachlorobiphenyl, octachlorostyrene) in Bermudian corals. *Mar Ecol Prog Ser* 16:149–154
- Spangenberg DB (1971) Thyroxine induced metamorphosis in *Aurelia*. *J Exp Zool* 178:183–194
- Stimson JS (1987) Location, quantity and rate of change in quantity of lipids in tissue of Hawaiian hermatypic corals. *Bull Mar Sci* 41:889–904
- Sullivan J, Ryan J, Watson J, Webb J, Mullikin J, Rokhsar D, Finnerty J (2006) StellaBase: the *Nematostella vectensis* genomics database. *Nucleic Acids Res* 34:D495–D499
- Takahashi T, Muneoka Y, Lohmann J, Lopez de Haro MS, Solleder G, Bosch TCG, David CN, Bode HR, Koizumi O, Shimizu H, Hatta M, Fujisawa T, Sugiyama T (1997) Systematic isolation of peptide signal molecules regulating development in hydra: LWamide and PW families. *Proc Natl Acad Sci USA* 94:1241–1246
- Tarrant AM (2005) Endocrine-like signaling in cnidarians: current understanding and implications for ecophysiology. *Integr Comp Biol* 45:201–214
- Tarrant AM, Atkinson S, Atkinson MJ (1999) Estrone and estradiol-17 β concentration in tissue of the scleractinian coral, *Montipora verrucosa*. *Comp Biochem Physiol* 122A:85–92
- Tarrant AM, Atkinson MJ, Atkinson S (2001) Uptake of estrone by a coral reef community. *Mar Biol* 139:321–325
- Tarrant A, Blomquist C, Lima P, Atkinson M, Atkinson S (2003) Metabolism of estrogens and androgens by scleractinian corals. *Comp Biochem Physiol* 136B:473–485
- Tarrant A, Atkinson M, Atkinson S (2004) Effects of steroidal estrogens on coral growth and reproduction. *Mar Ecol Prog Ser* 269:121–129
- Technau U, Rudd S, Maxwell P, Gordon P, Saina M, Grasso L, Hayward D, Sensen C, Saint R, Holstein T, Ball E, Miller D (2005) Maintenance of ancestral complexity and non-metazoan genes in two basal cnidarians. *Trends Genet* 21:633–639
- Tremblay M-E, Henry J, Anctil M (2004) Spawning and gamete follicle rupture in the cnidarian *Renilla koellikeri*: effects of putative neurohormones. *Gen Comp Endocrinol* 137:9–18
- Twan W-H, Hwang J-S, Chang C-F (2003) Sex steroids in scleractinian corals, *Euphyllia ancora*: implications in mass spawning. *Biol Reprod* 68:2255–2260
- Twan W-H, Hwang J-S, Lee Y-H, Jeng S-R, Yueh W-S, Tung Y-H, Wu H-F, Dufour S, Chang C-F (2006) The presence and ancestral role of GnRH in the reproduction of scleractinian coral, *Euphyllia ancora*. *Endocrinology* 147:397–406
- Walther M, Fleck J (1998) Synthetic peptides inducing metamorphosis in a tropical jellyfish: a quantitative structure–activity relationship study. *Comp Biochem Physiol* 120A:655–659
- Xian W, Kang B, Liu R (2005) Jellyfish blooms in the Yangtze Estuary. *Science* 307:41

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.