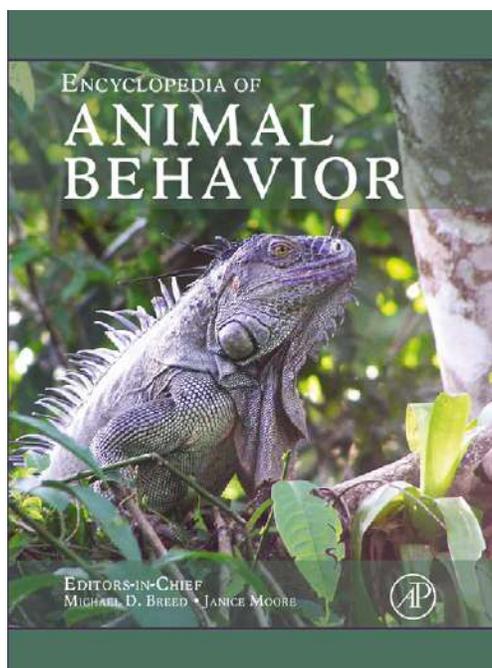


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Marine Invertebrates: Genetics of Colony Recognition

R. Grosberg and D. Plachetzki, University of California, Davis, CA, USA

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Introduction

Many sessile, encrusting clonal and colonial marine animals – notably sponges, cnidarians, bryozoans, and colonial ascidians – exhibit a suite of life-history traits that promote intraspecific competition for space and the evolution of complex behaviors that mediate the outcomes of somatic interactions. These traits include the capacity for *indeterminate growth* and reproduction, often augmented by limited dispersal and, in some cases, kin-directed settlement behavior of their sexual and asexual *propagules*. In these taxa, intraspecific competitive interactions elicit behaviors ranging from no apparent response, through active cytotoxic rejection, to intergenotypic fusion of individuals and colonies. Among cnidarians and some bryozoans, incompatibility responses extend beyond simple rejection, often eliciting a complex suite of agonistic behaviors. In addition, developmental transitions in the expression of these complex fusion and rejection behaviors may also occur.

As in many social insects and vertebrates that modify the expression of their social behaviors according to the relatedness of *conspecifics*, a growing number of field and laboratory studies on colonial marine invertebrates show that neither intergenotypic rejection and aggression, nor fusion randomly occur with respect to the genotypes of interacting conspecifics. Instead, the initiation of agonistic behavior often depends on the relatedness of contestants: interactions between clonemates and close kin generally do not elicit cytotoxicity or aggression, whereas interactions between more distant relatives do. Likewise, *somatic fusion* usually occurs only between clonemates and close kin. Thus, precise allorecognition, the ability to distinguish self from conspecific nonself, once thought to be the hallmark of the vertebrate immune system, is phylogenetically broadly distributed, and appears to be a ubiquitous feature of all multicellular animals, along with fungi, myxobacteria, and myxomycetes.

Pioneering studies of invertebrate allorecognition, dating back a century to classic studies on the colonial ascidian *Botryllus schlosseri*, made it clear that specificity in the expression of intercolony fusion and rejection was heritable. Thus, allorecognition in these taxa provided an early model for the studies of behavioral genetics. The dependence of *somatic rejection*, aggression, and fusion on relatedness, together with discrimination reliabilities that often exceed 95%, implies that (1) these behaviors enhance individual and *inclusive fitness* by mediating responses

with respect to the genetic identities of interactors; (2) genetically based recognition cues govern the expression of these behaviors; and (3) the diversity of these cues is built on unusually high levels of genetic variation.

In this way, several features of invertebrate allorecognition systems mirror several aspects of the major histocompatibility complex (MHC), a key element of the vertebrate adaptive immune system. For this reason, analogies between the vertebrate immune system and invertebrate allorecognition behavior inspired many early studies of invertebrate allorecognition, with the hope of discovering retained ancestral features of our own MHC. We now understand that most of the similarities between invertebrate allorecognition and vertebrate MHC systems are superficial and likely reflect convergent evolution, not common ancestry. Still, these parallels may reveal common selective forces that have led to the evolution of the diverse array of allorecognition systems, including the vertebrate MHC. For instance, the function of both allorecognition and the MHC relies on extremely high levels of genetic polymorphism that confer cue specificity. The use of highly *polymorphic*, genetically based phenotypic cues to regulate the expression of these social behaviors (including inbreeding avoidance) and immune function potentially imposes selection on the genes that produce these cues.

Understanding how natural selection influences the evolution of this exacting specificity and its underlying genetic diversity fundamentally requires an integrated analysis of both formal and molecular genetics of allorecognition. Formal genetic approaches generally involve breeding animals with different phenotypes, and then correlating the phenotypes of progeny with the presence or absence of genetic markers over successive crosses. In so doing, breeding studies can circumscribe how many loci are involved in the trait (i.e., how many distinct markers correlate with the allorecognition phenotype), the degree to which certain alleles are dominant over others in the expression of a given allorecognition phenotype, and the level of standing genetic variation that exists in a given population for an allorecognition phenotype (i.e., how many allorecognition classes, or *allotypes*, segregate in a population). Alternatively, studies on the molecular genetics of allorecognition can reveal the specific genes involved in these phenotypes and provide primary sequence-level resolution on the identity of loci involved in allorecognition. Such data make it possible to compare how alleles differ from each other, provide direct measures of how natural selection acts on individual loci, and

reveal how specific regions or positions within these loci evolve. In this way, formal and molecular genetic approaches complement each other and together offer powerful tools for deciphering the evolutionary genetics of allorecognition.

To this end, two marine invertebrate model systems have emerged over the last two decades, one focusing on the colonial ascidian genus *Botryllus* (Phylum Chordata), and the other on colonial hydrozoans in the genus *Hydractinia* (Phylum Cnidaria). In both these cases, formal and molecular genetic approaches have begun to reveal key components of the allorecognition machinery. These components minimally include the genes encoding receptors and cues that determine behavioral responses to other conspecifics. Here, we summarize what is presently understood about the genetics of allorecognition in these two taxa, along with the far more limited data that presently exist for bryozoans and sponges. We also evaluate the functional significance of allorecognition in colonial marine invertebrates and consider how various forms of natural selection can explain what is presently understood of the genetics of allorecognition. Finally, we review the broad *macroevolutionary* patterns of allorecognition behavior in colonial invertebrates and consider the factors that may have contributed to their evolution.

Genetics of Allorecognition in *Botryllus schlosseri*

The formal and molecular genetics of allorecognition are better understood in the colonial ascidian *B. schlosseri* than in any other invertebrate system. Ascidiates are soft-bodied invertebrate chordates (Phylum Chordata) that belong to the Subphylum Tunicata, a clade that diverged from its sister taxon, the Craniata (including the vertebrates), over 600 Ma. The life cycles of botryllid ascidians such as *B. schlosseri* offer many opportunities for allorecognition behavior to be expressed. First, the fertilized egg develops into a motile tadpole-like larval stage. This tadpole stage possesses all the diagnostic chordate features, including a notochord, a dorsal hollow nerve tube, and pharyngeal gill slits. The larvae swim for a few minutes to hours, and then attach to hard substrates, often dispersing so little that they settle in the vicinity of their kin, apparently using shared allorecognition alleles to detect their relatives. Once attached, the tadpole metamorphoses into a minute, founding oozoid. During the metamorphic transition to an attached phase, the juvenile *Botryllus* loses all its chordate features, except for its gill slits, which it uses for respiration and feeding. The oozoid then asexually buds off additional zooids (Figure 1(a)), which in turn bud still more zooids. Repeated cycles of asexual budding ultimately give rise to a modular colony of genetically identical zooids, each with its own set of ovaries and testes. The zooids lie embedded in a

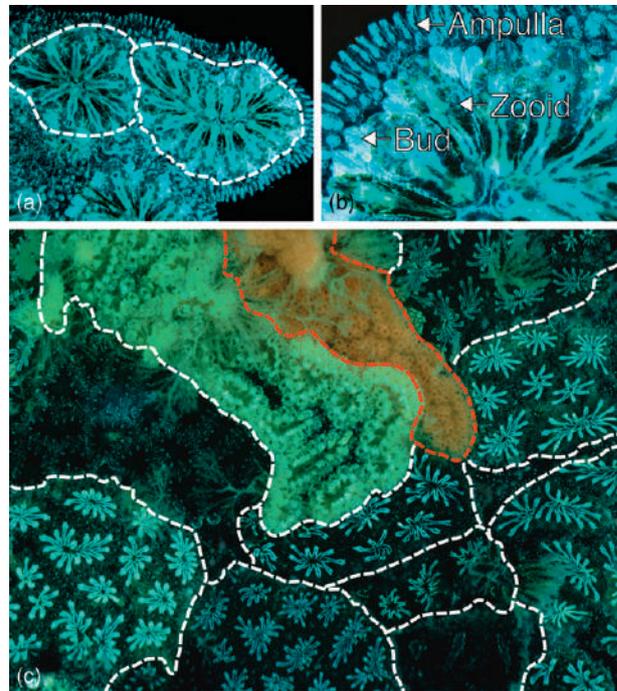


Figure 1 Colony structure and ecology of the colonial ascidian *Botryllus schlosseri*. (a) The adult zooids (the modular, cloned units that compose a colony) of *B. schlosseri* form star-shaped systems embedded in a gelatinous tunic. Numerous tiny saccular ampullae of the tunic's interzooidal blood-circulatory complex fringe the colony's complex blood vascular system. (b) A group of adult zooids, asexual buds (which sequentially and synchronously develop into new zooids), and peripheral finger-like projections of the blood-vascular system called 'ampullae' (sites of allorecognition). (c) Competition for spatial resources is fierce. Individual colonies of *B. schlosseri* (outlined in white dashed lines) surrounding a single colony of *Botrylloides leachi*, a species closely related to *Botryllus* (red dashed lines).

cellulose matrix (the tunic), interconnected by a ramifying and anastomosing blood vascular system (Figure 1(b)). Colony size has no intrinsic physiological or structural limit; consequently, *B. schlosseri* colonies can continually grow, often encountering themselves (self-recognition) or conspecifics (allorecognition) as they expand (Figure 1(c)). When colony edges meet, they interact via ampullae, finger-like projections of their vascular network (Figure 2(a)). The ampullae may either fuse, establishing blood flow between the colonies, or reject, a response accompanied by cytotoxic reactions and the formation of a barrier between incompatible colonies.

Extensive breeding studies, dating back to the early 1960s, show that the outcome of these interactions – fusion or rejection – depends on a single highly polymorphic allorecognition locus, now called *FuHC*. Alleles at *FuHC* are expressed codominantly in *Botryllus*. Upon contact, individuals that share one or both alleles at *FuHC* fuse (Figure 2(b)), whereas pairs of colonies that do not share an allele reject (Figure 2(c)). The DNA sequence of *FuHC*

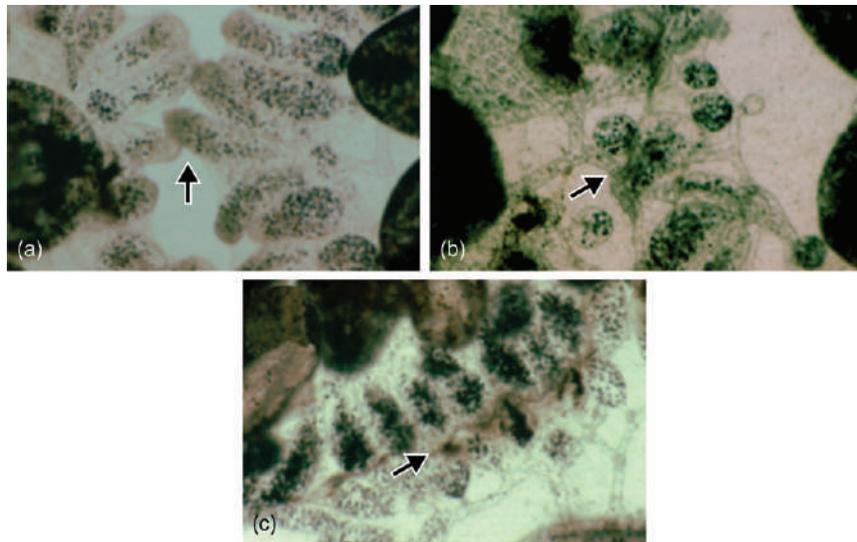


Figure 2 Allorecognition reactions in *Botryllus schlosseri*. (a) Initial contact between the ampullae of two colonies. (b) Vascular fusion between two colonies that share one or both alleles at their *FuHC* locus. (c) Cytotoxic rejection between two incompatible colonies that lack a shared *FuHC* allele. Arrows denote initial points of contact.

shows no obvious homology to any known vertebrate gene. Nevertheless, like other genetic systems mediating allorecognition, the *FuHC* locus displays an extreme level of allelic variation, with several studies yielding estimates of polymorphism in excess of 100 alleles, and heterozygosities that approach 1. These extraordinary levels of genetic polymorphism mean that individuals are only likely to share alleles with themselves (self) and close relatives; thus, this polymorphism permits individuals to discriminate kin relationships with far greater resolution than if fewer alleles were present in the population. Also, because only a single shared *FuHC* allele is required for fusion, individuals that are only related as kin, not clones, can fuse. Thus, genetic chimeras (single colonies composed of multiple genotypes) arise with appreciable frequency in *Botryllus*, but are only likely to form between close kin.

Other loci in addition to *FuHC* may be involved in histocompatibility and allorecognition responses in *Botryllus*. The same genetic mapping and functional approaches that revealed the identity of the *FuHC* locus also hinted at another locus involved in allorecognition. This locus, called *fester*, is polymorphic, though to a lesser extent than *FuHC*. However, in addition to sequence polymorphisms, *fester* expresses a large number of unique mRNA splice products that yield a higher diversity of *fester* gene products in the population than would be expected from allelic diversity alone.

What is the evidence that *fester* functions with *FuHC* to mediate allorecognition behavior in *B. schlosseri*? First, in adult *B. schlosseri* *fester*, gene expression is restricted to the ampullae (the site of either fusion or rejection) and to a subset of blood cells thought to play an important role in allorecognition. Furthermore, *B. schlosseri* can express

allorecognition behavior as early as the tadpole larval phase, and both *fester* and *FuHC* share a common domain of gene expression in early tadpole and oozoid developmental stages. Most compelling is the fact that knocking down the expression of *fester* produces altered allorecognition phenotypes. It seems that *fester* is a receptor for *FuHC* gene products; however, its exact role in allorecognition is still uncertain.

Genetics of Allorecognition in *Hydractinia symbiolongicarpus*

The cnidarian genus *Hydractinia* encompasses a clade of marine, colonial hydrozoans, many of which inhabit the discarded shells of marine gastropods that are subsequently occupied by hermit crabs (Figure 3(c), inset). Like *Botryllus*, several species in this genus have relatively short generation times (on the order of weeks to months) and can be cultured and bred in the lab, making them ideal candidates for the genetic studies of allorecognition behavior. Colonies of *Hydractinia* are either male or female: males shed sperm into the water, and fertilized eggs develop into minute, wormlike larvae (planulae) while held on the female colony. When a crawling planula contacts a hermit shell, it metamorphoses into a founder polyp, analogous to the oozoid of *Botryllus*. Through repeated episodes of asexual budding, a colony develops, which – in the absence of competitors – could expand to cover the entire shell. However, in many cases, multiple sexually produced planulae colonize a single shell, and the ensuing intraspecific competition for space may be fierce.

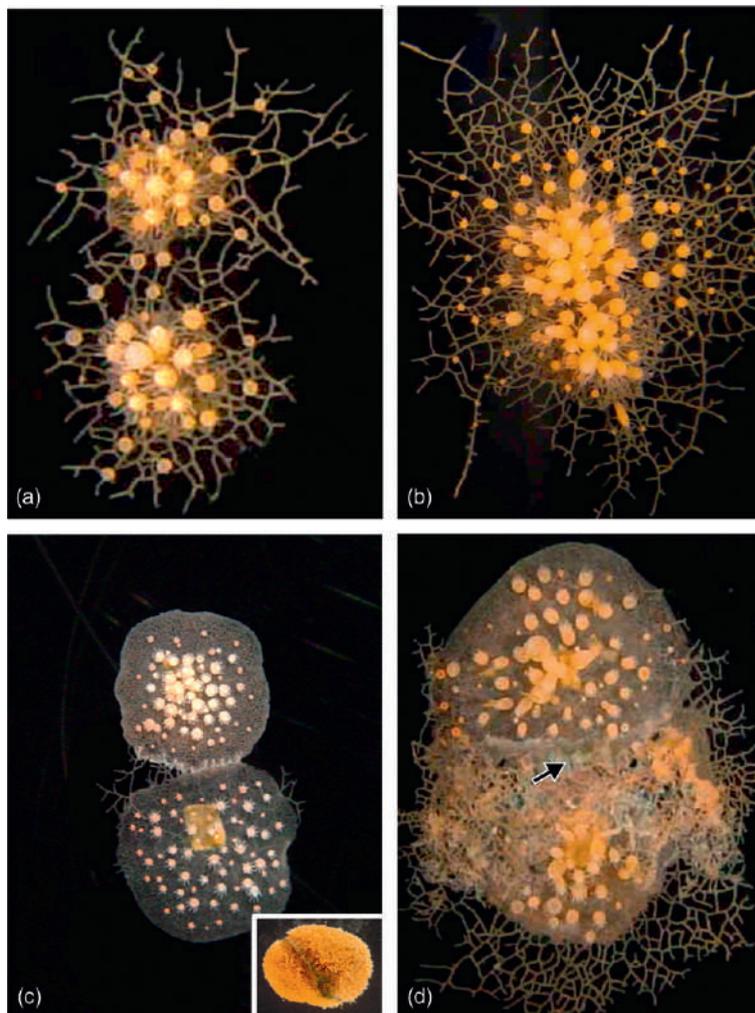


Figure 3 Fusion and rejection responses in *Hydractinia symbiolongicarpus*. (a and b) Fusion between compatible colonies, in this case, full siblings. (c and d) Aggressive rejection between incompatible colonies, accompanied by the production of nematocyst-laden hyperplastic stolons (arrow). (b and d) were taken 2 weeks after (a) and (c), respectively. Inset, a hermit-crab-occupied snail shell colonized by two incompatible *H. symbiolongicarpus* colonies, separated by a conspicuous zone of rejection.

As *Hydractinia* colonies grow, they extend tubelike stolons over the shell, from which specialized feeding, defensive, and reproductive polyps, emerge. The stolons themselves are extensions of the guts of each of the polyps and form a gastrovascular system that links the members of a colony. When a colony encounters itself as it grows around a shell, its stolons invariably fuse, preserving the integrity of self and functionally unifying the colony. When the stolons of genetically distinct colonies grow into contact, one of the three outcomes ensues: (1) fusion, forming a functionally and behaviorally integrated, but genetically chimeric individual (**Figure 2(a)** and **2(b)**); (2) aggressive rejection, accompanied by the induction of specialized organs of aggression, the hyperplastic stolons (**Figure 2(b)** and **2(c)**); or (3) transitory fusion, in which initial fusion is followed by varying degrees of rejection. As with *Botryllus*, the probability of fusion is closely tied to kinship: parents

and offspring invariably fuse, but full sibs usually fuse < 40% of the time, and more distantly, relatives are rarely compatible, and usually aggressively reject each other.

With aggressive rejection, closely apposed stolons begin to accumulate specialized *nematocytes*, the diagnostic stinging cells of cnidarians, to their tips, and become hyperplastic. Interestingly, the recruitment of nematocytes to form hyperplastic stolons begins before rejecting individuals actually touch, suggesting the action of a diffusible chemical cue that signals allotypic identity or disparity. By some unknown trigger, nematocytes from one of the hyperplastic stolons synchronously discharge, injuring, and sometimes, eventually killing an opponent. Alternatively, aggressive bouts can persist as standoffs for weeks or months with no clear winner.

Despite over half a century of research on allorecognition in *Hydractinia*, the genetic basis of specificity

is just beginning to be understood. Early accounts suggested that a single genetic locus with multiple codominant alleles controlled allorecognition specificity, as in *Botryllus*. However, subsequent genetic models and mating studies confirmed that multiple loci likely control allorecognition, at least in *Hydractinia symbiolongicarpus*. One recent study, using highly inbred lines, implicated two distinct genetic loci, *alr1* and *alr2*, that cosegregated with allorecognition phenotypes. *Positional cloning* of the genomic region that contained these markers showed that *alr2* is an immunoglobulin-like protein with both transmembrane and hypervariable amino acid sequence regions, making *alr2* a candidate allorecognition surface protein. If *alr2* is an allorecognition surface protein, the role that *alr1* plays in mediating allorecognition in *Hydractinia* remains to be determined.

In contrast to our understanding of the genetic basis of allorecognition in *Botryllus*, a correlation between specific polymorphisms at these loci and the expression of allorecognition phenotypes has not yet been fully demonstrated. Much of the confusion over this question relates to the fact that key experiments have yet to be conducted in the *Hydractinia* system. For instance, the power of our understanding of the genetics of allorecognition in *Botryllus* stems from experiments where wild-caught (non-inbred) individuals were tested against lab strains that had been characterized at the *FuHC* locus. Importantly, both fusion and rejection phenotypes were observed in these allorecognition experiments allowing the sequences at *FuHC* to be correlated with the observed phenotypes. Similar experiments need to be conducted in *Hydractinia*. Furthermore, the types of functional assays that were pivotal to demonstrating that *FuHC* is an allorecognition locus in *Botryllus* have yet to be performed in *Hydractinia*.

Once candidate genes are identified by formal and molecular genetic analysis, the best standards of evidence linking these genes to specific allorecognition phenotypes are gain- and loss-of-function experiments. Here, the hypothesis that a specific gene is involved in the expression of a given phenotype (for instance, allorecognition) is tested by turning off the function of the specific gene and assessing any change that results in phenotype. Changes that do occur may then be 'rescued' by turning the gene of interest back on. Such experiments, commonly referred to as functional genomics, are often done using gene knock-down methodologies that include RNA interference (RNAi), morpholinos, and other methods. Irrespective of the method used, these techniques allow the hypothesis that a specific gene of interest is involved in an observed phenotype to be tested directly. Although the *alr1* and *alr2* loci are likely to be involved in *Hydractinia* allorecognition, functional genomics experiments are the crucial next steps toward understanding the genetics of allorecognition in this system.

Genetics of Other Allorecognition Systems

As we have seen, the life histories of many colonial marine invertebrates make allorecognition a critical aspect of their behavior and ecology. In addition to colonial ascidians and hydrozoans, many sponges, bryozoans, and anthozoan cnidarians such as anemones and corals are capable of precise allorecognition. Sponges and bryozoans tend to exhibit fusion-rejection behaviors like those of colonial ascidians, with rejection associated with cytotoxicity, and the preservation of the genetic integrity of self, but not the induction of behaviors or structures that are overtly agonistic. On the other hand, as in *Hydractinia*, incompatibility in many anthozoan cnidarians is often accompanied by the production of aggressive structures, heavily armed with specialized nemaotocysts, that include modified tentacles (e.g., sweeper tentacles and acrorhagi), extensions of the gut (e.g., mesenterial filaments), and entire polyps (e.g., dactylozooids).

While a great deal is known about the occurrence of allorecognition behaviors in sponges, corals and anemones, and bryozoans, the challenges of breeding most colonial marine invertebrates in the lab have left the formal and molecular genetics of allorecognition in taxa, other than *Botryllus* and *Hydractinia*, virtually unknown. Consequently, most studies of the relationship between fusion and rejection frequencies and relatedness involve various proxies for kinship, often distance between sources of experimentally grafted colonies. Because both sexually and asexually produced propagules in most colonial marine invertebrates have relatively limited dispersal potential, kinship should decline with the distance separating two individuals.

For example, in the Pacific sponge *Calkyspongia* (Phylum Porifera), grafting experiments show that the likelihood of fusion between fragments increases as the distance between source colonies decreases. Similar patterns of fusion frequencies declining with distance are well documented in other sponges; however, it is often unknown whether compatible grafts are limited to clonal fragments, or whether kin can fuse as well. Allorecognition also occurs in colonial, encrusting bryozoans (suspension-feeding members of the *Lophotrochozoa*). In many bryozoans, sexually produced larvae are shed into the water column daily. In some species with nonfeeding larvae, settlement habitually occurs near the parental colony. And, as in *Botryllus*, the larva of at least one species of bryozoan seems to take relatedness into account when making their settlement decisions. Analyses of fusion and rejection in several bryozoans and many corals and sponges confirm the general pattern that clonemates are always compatible, and that compatibility declines with relatedness between allogeneic individuals.

Evolution of Allorecognition Systems

The specificity of fusion and rejection behaviors in all colonial marine invertebrates studied to date suggests that the loci controlling allorecognition specificity are extremely polymorphic. This raises two questions: (1) what is the source of the underlying genetic variation? and (2) how are such high levels of polymorphism maintained in natural populations? In terms of sources of variation, simple nucleotide substitutions may generate most of the observed allelic variation. But there are other ways by which hypervariable recognition cues could be generated, one likely candidate being the structural alteration of genetic loci themselves via *somatic recombination*. Examples of this polymorphism-generating mechanism include intraindividual genomic recombination, as is the case for the V(D)J system in the vertebrate adaptive immune system, and the generation of alternative splice products, as is the case for the *fester* locus in the *Botryllus* allorecognition system. These changes to the physical structure of genes or mRNA transcripts represent direct polymorphism-generating mechanisms, but examples of such mechanisms are rare.

It seems inescapable that some form of selection favoring rare alleles (negative frequency-dependent selection) drives the maintenance of the extreme levels of polymorphism inferred in most populations of marine invertebrates. The expression of behaviors such as fusion and rejection in colonial marine invertebrates is obviously functionally important, both in terms of the maintenance of the genetic integrity of self (and avoiding the costs of various forms of somatic and germ line parasitism that 'defector' genotypes may inflict on their fusion partners) and competition for space. By limiting fusion to clonemates and close kin, highly polymorphic allorecognition systems minimize the possibility of fusing with a parasitic genotype and maximize the inclusive fitness benefits of behaving altruistically toward a fusion partner. In cnidarians especially, by directing aggressive behavior away from clonemates and close kin, allorecognition systems reduce the inclusive fitness costs of harming self or a relative.

In *Botryllus*-like systems where the genetics of allorecognition determine whether intergenotypic contacts elicit fusion or passive rejection, simple population genetic models confirm our intuition that rare allorecognition alleles will be favored when the costs of intergenotypic fusion exceed the benefits. These costs include various forms of intraspecific parasitism, whereas the benefits of fusion include enhanced competitive ability or a greater range of environmental tolerance arising from increased genetic diversity in chimeric individuals. However, the situation is more complicated and daunting when aggression, rather than merely passive rejection, is an alternate outcome to fusion. The paradox arises

because any new mutant, that by definition must be initially rare, will face nearly universal assault from more common allotypes. For this reason, it is hard to imagine how rare allotypes could increase in frequency and become established in a population. There are several ways that selection might circumvent this obstacle. For one, as we have seen, populations of colonial invertebrates are often not randomly distributed spatially with respect to relatedness among individuals: kin are far more likely to interact than would be expected if there were extensive dispersal of motile larval and asexual propagules. Consequently, a newly arising allotype might encounter kin with appreciable frequency, decreasing the risks of attack and at least allowing an initial increase in the frequency of a rare mutant. Alternatively, selection favoring rare alleles for some other phenotype, that is, mating and inbreeding avoidance as in mice and perhaps other mammals, or in disease resistance, could initially favor allotypes that could subsequently be employed as allorecognition markers.

Phylogenetic Distribution of Allorecognition in Colonial Invertebrates

Allorecognition systems are distributed widely across the animal tree of life. Sponges, bryozoans, ascidians, and colonial hydrozoans each occupy distinct branches on this tree, and have likely been on their own independent evolutionary pathways for well over half a billion years (Figure 4). The extremely divergent phylogenetic distribution of allorecognition and the absence of clearly shared genetic elements in the systems that have been explored thus far on the molecular level (e.g., the *FuHC* and *fester* genes in *Botryllus*, the *alr1* and *alr2* genes of *Hydractinia*, and the vertebrate MHC genes) suggest one of the two possibilities for the macroevolutionary distribution of allorecognition behaviors. Either they are so distantly related that the signature of common ancestry has been lost (the last common ancestor of sponges and ascidians may have existed as many as 1 billion years ago), or the different allorecognition systems have evolved independently in animals.

Most modern views of animal phylogenetic relationships place the sponges as the earliest branching metazoan lineage. Sponges possess several highly specialized cell types, but lack tissue-grade organization. If the diversity of animal allorecognition systems evolved from a common ancestor that predated sponges, it could have done so to mediate interactions between the cells of isogenic and allogeneic individuals. Such interactions occur in modern sponges (not to mention myxobacteria, many fungi, red algae, and cellular slime molds) and can give rise to genotype-specific partitions of sponge cell types in chimeric individuals. Indeed, the ability to distinguish

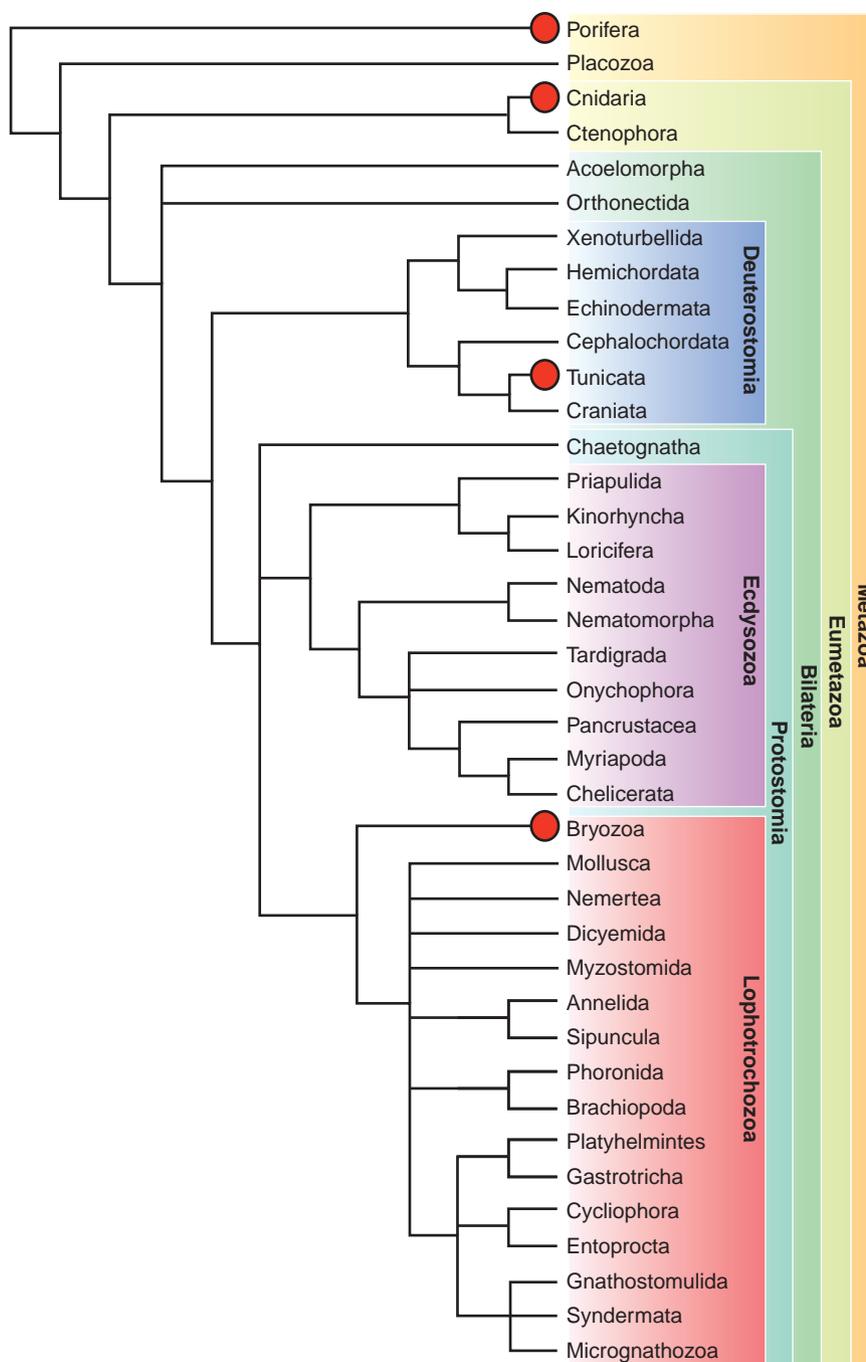


Figure 4 One recent view of animal phylogeny showing the distribution of all-recognition behavior (red circles). Much of the living phyletic diversity of animals can be found in the three major clades of bilaterian animals (deuterostomes, ecdysozoans, and lophotrochozoans). Earlier branching lineages include sponges (Porifera) and cnidarians. That all-recognition occur across such vast phylogenetic intervals may indicate the independent origins of these systems.

conspecific self from nonself extends well beyond the evolutionary history of animals and appears to be a basic attribute of multicellular life.

All all-recognition systems may have evolved several billion years ago from a common ancestor to the three major domains of life. However, it seems far more likely that all-recognition evolved multiple times in the deep

history of multicellular life and occurred independently in the four major groups discussed here. If so, the evolution of all-recognition behavior in disparate lineages represents an incisive and fundamental example of convergent evolution of a behavioral phenotype. The organismal, behavioral, and ecological attributes shared among these taxa (e.g., indeterminate growth, asexual propagation, and

limited dispersal) may have provided the adaptive substrate for the independent evolution of allorecognition in disparate lineages. However, only when we understand the genetics that underlie these behaviors in greater depth can we discriminate between these alternatives.

Conclusions

Allorecognition is a conditional behavior whose expression depends not only on the genotypes of both participants in an interaction, but also, as several studies on hydrozoans and corals suggest, on their developmental state. This, in and of itself, makes characterizing phenotypes and their underlying genotypes a major challenge. In addition, many of the organisms that exhibit allorecognition-dependent behaviors are long lived and difficult to culture in the lab, posing major challenges to developing the kind of broad taxonomic coverage that promises to reveal underlying functional and genetic patterns.

Nevertheless, several clear patterns do emerge. For instance, virtually all known allorecognition systems have very high specificity, which is presumably controlled by numerous variable genetic factors. In addition, despite the fact that such specificity could be controlled by genetic variation distributed across many loci, what we presently understand from the *Botryllus* and *Hydractinia* systems suggests that just a few loci with extensive allelic variation at each locus controls specificity. This pattern could reflect functional constraints on (1) the genes that confer specificity, (2) co-evolution between the genes that confer specificity (cues) and those that actually encode the receptors that facilitate recognition, or, (3) the genes that mediate how cues and receptors interact to yield specific behaviors such as somatic fusion and rejection. Finally, it appears that only partial genetic matching is necessary for two allotypes to be compatible; in other words, the available evidence suggests that self is recognized, rather than nonself. Whether this reflects recognition errors, or selection favoring the ability to distinguish not just self from nonself, but close from distant kin, continues to be a matter of considerable debate.

Regardless of whether individual or kin recognition is the primary selective factor favoring the evolution of genetic diversity in allorecognition systems, growing

evidence from many groups of multicellular organisms confirms that the capacity to distinguish self from nonself may be a universal and essential feature of multicellular life. The genetic data currently available suggest that allorecognition evolved numerous times in the history of life, and was likely co-opted in many different ways to regulate the expression of traits such as agonistic behavior, mating preferences, and pathogen defense.

See also: *Dictyostelium*, the Social Amoeba; Kin Recognition and Genetics; Recognition Systems in the Social Insects; Social Insects: Behavioral Genetics.

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